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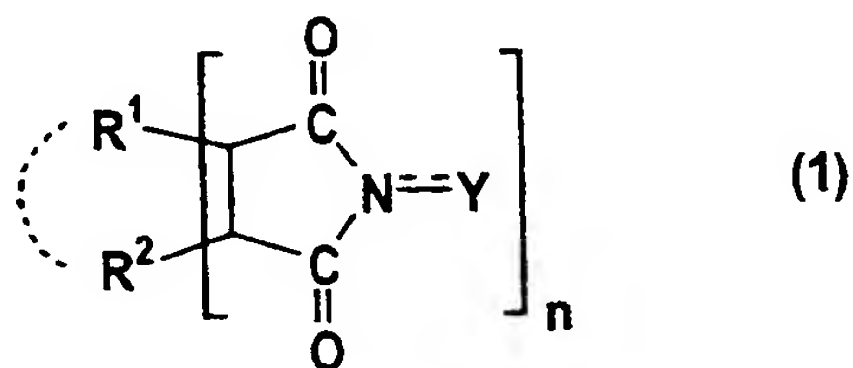
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(54) NITRATION OR CARBOXYLATION CATALYSTS

(57) In the presence of an imide compound (e.g., N-hydroxyphthalimide) shown by the following formula (1):



wherein R¹ and R² represent a hydrogen atom, a halogen atom, an alkyl group, an aryl group and a cycloalkyl group, and R¹ and R² may bond together to form a double bond, or an aromatic or non-aromatic ring, and Y is an O or OH, and n denotes 1 to 3; a substrate is allowed to contact with at least one reactant selected from (i) a nitrogen oxide and (ii) a mixture of carbon monoxide and oxygen to be introduced with at least one functional group selected from a nitro group and a carboxyl group. The nitrogen oxide includes, for

example, a compound represented by the formula N_xO_y (e.g., N₂O₃, NO₂). The substrate includes, for example, a compound having a methine carbon atom (e.g., adamantane), a compound having a methyl group or a methylene group at an adjacent moiety of an aromatic ring. According to such reaction, the substrate can be efficiently nitrated or carboxylated even in a mild or moderate condition.

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Description

TECHNICAL FIELD

5 [0001] The present invention relates to a catalyst useful for directly and efficiently nitrating and/or carboxylating a substrate by using at least one reactant selected from (i) a nitrogen oxide and (ii) a mixture of carbon monoxide and oxygen, and a compound obtained by using the catalyst and a process for producing the compound (a nitration/carboxylation process, a process for producing a compound having a nitro group and/or carboxyl group, a novel adamantane derivative, and a process for producing an adamantane derivative) using the catalyst.

10

BACKGROUND ART

[0002] Nitro compounds are commonly utilized as a raw material for medicine, agricultural chemicals, dyes, solvents and explosives, a raw material for amino compounds, and the like. Moreover, carboxylic acids (carboxy compounds) are useful as a raw material of a variety of compounds such as esters. Among them, dicarboxylic acids are useful as a raw material of polyesters.

15 [0003] Nitration of hydrocarbons is generally conducted by a nitric acid process which employs a mixed acid (a mixture of nitric acid and sulfuric acid). However, the nitric acid process requires a strong acid with high concentration in a large amount. Besides, since the nitration reaction is exothermic, it is difficult to improve its reaction operability. Furthermore, in the nitric acid process, large amounts of nitrogen oxides produce, which cause environmental pollution and thus have to be treated in a proper manner.

20 [0004] As a nitration process, use of N_2O_5 and ozone in the presence of an iron catalyst has been suggested for nitration of aromatic compounds (e.g., toluene) or alicyclic compounds (e.g., adamantane). Due to the use of NO_3 as a reactant, this nitration process can proceed smoothly at a lower temperature. However, a catalyst should be incorporated in order to increase the reaction rate, and additional equipment such as an ozone-generating apparatus should be installed for the generation of ozone.

25 [0005] Carboxyl compounds (e.g., phthalic acid) can be obtained by, for example, an oxidation of a substrate (e.g., naphthalene). In Such oxidation reaction, a carboxyl compound having carbon atoms fewer than a substrate can be usually obtained. Moreover, in order to obtain a carboxyl compound of a bridged cyclic hydrocarbon (e.g., 1-carboxyladamantane) by an oxidation reaction, it is required that a group which can be converted to a carboxyl group by oxidation (e.g., methylol group) is introduced to a methine carbon atom, and then the methine carbon atom is oxidized. It is considerably difficult.

30 [0006] As a carboxylation process of a hydrocarbon compound, for example, a process for providing a carboxylic acid by using Grignard reaction is broadly known. In this process, many reaction steps are required since a substrate can not be directly carboxylated and include that a special compound such as an organic metal compound (e.g., a Grignard compound) is previously prepared from a substrate, carbon dioxide is allowed to act on the organic metal compound, and the organic metal compound is hydrolyzed to be carboxylated. Further, it is difficult to prepare the organic metal compound, additionally the compound is not convenient to handle.

35 [0007] Japanese Patent Application Laid-open No.38909/1996 (JP-A-8-38909) discloses a process which comprises contacting a substrate with oxygen to oxidize in the presence of an imide compound such as N-hydroxyphthalimide to provide a corresponding oxide (e.g., a carboxylic acid). In this process, a process for producing adipic acid from cyclohexane is described. In this process, a carboxyl compound having the same number of carbon atoms as a substrate can be obtained usually.

40 [0008] On the other hand, adamantane has a three-dimensionally symmetric structure and skeletons which insure mutual stabilization of each ring, and as a result, endowed with distinctive functions. Various highly functionalized copolymers can be obtained, for example, by introducing a functional group such as a carboxyl group or an amino group to adamantane and optionally deriving to other derivatives thereof. There have been proposed various production processes for obtaining such copolymers from a functional group-introduced adamantane derivative. The processes include, for example, a process of producing a polyester [e.g., Japanese Patent Application Laid-open No. 21090/1975 (JP-A-50-21090)], a process of producing a polycarbonate [e.g., U.S. Patent No. 3,594,427], a process for producing a polyamide or a polyimide [e.g., U.S. Patent No. 3,832,332], a process for producing a polyurethane [e.g., Japanese Patent Publication No. 12891/1969 (JP-B-44-12891)], a process for producing a polysulfone and a polysulfonate [e.g., U.S. Patent No. 3,753,950], and a process for producing a vinyl polymer [e.g., Japanese Patent Publication No. 28419/1971 (JP-B-46-28419)].

45 [0009] These polymers provided from an adamantane derivative have generally excellent functions or characteristics (high functionality). They have, for example, optical characteristics such as small light-inducing loss, high refractive index, double refraction index, excellent characteristics such as moisture resistance, excellent heat resistance (heat resisting property) and thermal expansivity. Such excellent characteristics cannot be achieved with the use of conven-

tional polymers. Accordingly, applications of said polymer have been investigated for optical materials such as optical fibers, optical elements, optical lenses, hologram, optical discs, and contact lenses, transparent resin coating compositions for organic glasses, electric conductive polymers, photosensitive materials, fluorescent materials and so forth.

[0010] On the other hand, an amino derivative derived from an alcohol of an adamantane is useful for introducing various pharmaceuticals and/or agricultural chemicals each having excellent pharmacological activity, and is used as a therapeutic agent for Parkinson's disease such as "SYMMETREL" (a trade name). A diamino body of adamantane is useful as an intermediate material for antibacterial drugs (agents) or antiviral drugs (agents).

[0011] The above mentioned diamino body (diamino form) of the adamantane is produced by aminating a dihalo body obtained by halogenating a diol body of an adamantane. However, in a process for the formation of a salt of the diamino body obtained by aminating the dihalo body of adamantane, a side reaction tends to occur, additionally it is difficult to separate and collect a free diamino body in a high yield.

[0012] It is, therefore, an object of the present invention to provide a catalyst which can efficiently nitrate and/or carboxylate a substrate, and a nitration and/or carboxylation process using the catalyst.

[0013] It is another object of the present invention to provide a catalyst which can nitrate or carboxylate a substrate by using at least one reactant selected from (i) a nitrogen oxide and (ii) a mixture of carbon monoxide and oxygen even in a mild or moderate condition, and a nitration and/or carboxylation process of a substrate using the catalyst.

[0014] A further object of the present invention is to provide a catalyst which can provide a compound having at least one functional group selected from nitro group and carboxyl group with high conversion and selectivity, and a process for producing the compound having a functional group by using the catalyst.

[0015] Another object of the present invention is to provide a process for nitration which can utilize effectively nitrogen oxides, which cause environmental pollution, for providing nitro compounds with high conversion and selectivity.

[0016] Further object of the present invention is to provide a process for producing a carboxyl compound which has more carbon atoms than the number of carbon atoms of a substrate, efficiently with simple operation at fewer steps.

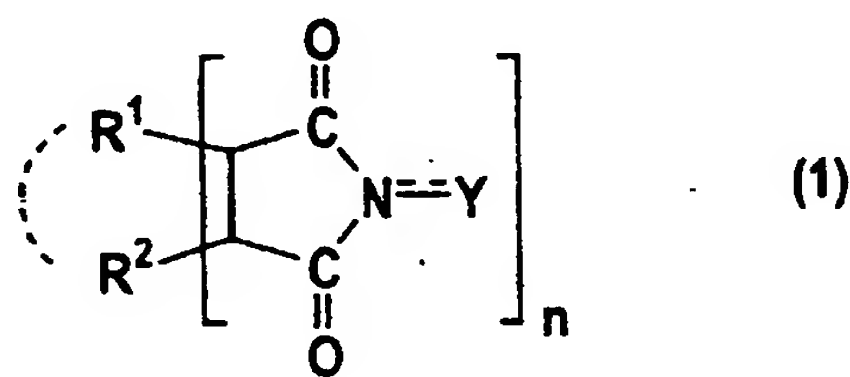
[0017] Still further object of the present invention is to provide a novel adamantane derivative.

[0018] Still another object of the present invention is to provide a process which can produce a diamino body of adamantane in high yield.

DISCLOSURE OF INVENTION

[0019] The inventors of the present invention did intensive investigation to accomplish the above objects, and finally found that a reaction of at least one reactant selected from (i) a nitrogen oxide (e.g., N_2O_3 , N_2O) and (ii) a mixture of carbon monoxide and oxygen with a substrate in the presence of a catalyst comprising a specific imide compound, efficiently introduce at least one functional group selected from a nitro group and a carboxyl group to the substrate and that useful adamantane derivatives including a novel adamantane derivative can be produced by using the above method.

[0020] Thus, a catalyst of the present invention is for introducing at least one functional group selected from a nitro group or a carboxyl group to a substrate by contacting the substrate with at least one reactant selected from (i) a nitrogen oxide and (ii) a mixture of carbon monoxide and oxygen to and comprises an imide compound shown by the following formula (1):



wherein R^1 and R^2 may be the same or different from each other, and represent a hydrogen atom, a halogen atom, an alkyl group, an aryl group, a cycloalkyl group, a hydroxyl group, an alkoxy group, a carboxyl group, an alkoxy-carbonyl group, and an acyl group, and R^1 and R^2 may bond together to form a double bond, or an aromatic or non-aromatic ring; Y represents an oxygen atom or a hydroxyl group; and n denotes an integer of 1 to 3.

[0021] The catalyst may comprise the imide compound shown by the formula (1) and a co-catalyst. As the co-catalyst, there may be employed, for example, a compound containing at least one element selected from the group consisting of Group 2A elements of the Periodic Table of Elements, transition metal elements and Group 3B elements of the Periodic Table of Elements.

[0022] According to the process of the present invention, in the presence of the imide compound shown by the formula (1), or the imide compound and the co-catalyst, a substrate is allowed to contact with at least one reactant selected from

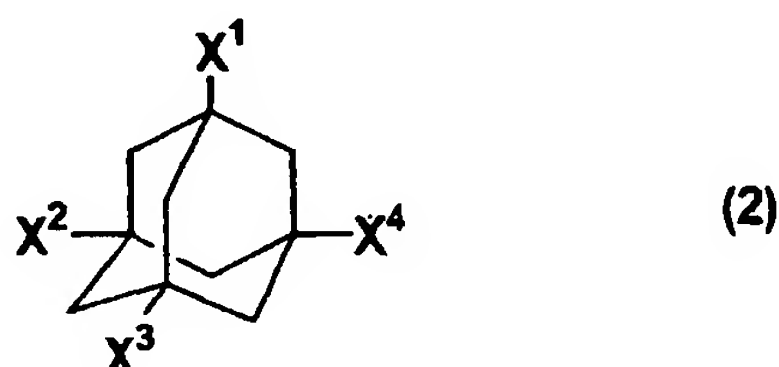
(i) a nitrogen oxide and (ii) a mixture of carbon monoxide and oxygen to introduce at least one functional group selected from a nitro group and a carboxyl group to the substrate. The substrate includes, for example, (a) a compound having a methyl group or a methylene group at an adjacent site of an unsaturated bond, (b) a homo- or hetero cyclic compound having a methylene group, (c) a compound having a methine carbon atom, (d) a compound having a methyl group or a methylene group at an adjacent site of an aromatic ring and (e) a compound having a methylene group at an adjacent site of a carbonyl group. As the nitrogen oxide, there may be employed, for example, a compound shown by the formula:



wherein x denotes an integer of 1 or 2 and y denotes an integer of 1 to 6; such as N_2O_3 , NO_2 .

[0023] The present invention comprises a process for producing a compound having at least one functional group selected from a nitro group and a carboxyl group by using the above process, as well.

[0024] A novel adamantane derivative of the present invention is a compound shown by the following formula (2) or (3):



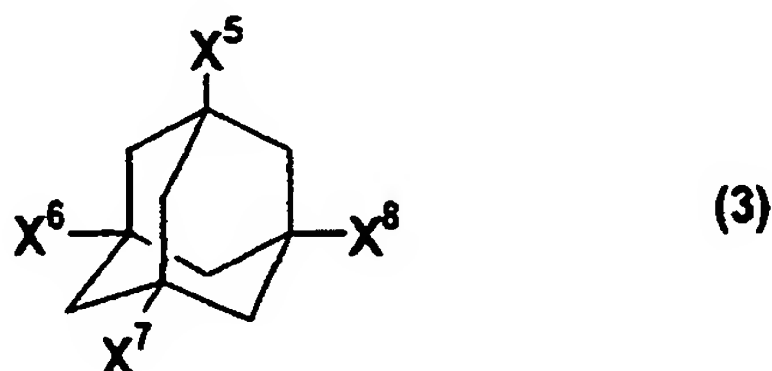
wherein X^1 represents a nitro group, an amino group or N-substituted amino group which may be protected by a protective group, a carboxyl group which may be protected by a protective group, or a hydroxymethyl group which may be protected by a protective group; and X^3 and X^4 may be the same or different from each other, and represents a hydrogen atom, an alkyl group, a nitro group, an amino group or N-substituted amino group which may be protected by a protective group, a carboxyl group which may be protected by a protective group, a hydroxymethyl group which may be protected by a protective group or an isocyanato group;

(i) when X^1 is a nitro group, X^2 represents an amino group or N-amino group which may be protected by a protective group, a hydroxymethyl group which may be protected by a protective group, or an isocyanato group;

(ii) when X^1 is an amino group or N-substituted amino group which may be protected by a protective group, X^2 represents an isocyanato group;

(iii) when X^1 is a carboxyl group which may be protected by a protective group, X^2 represents a hydroxymethyl group which may be protected by a protective group, or an isocyanato group; and

(iv) when X^1 is a hydroxymethyl group which may be protected by a protective group, X^2 represents an isocyanato group;



wherein X^5 represents a carbamoyl group which may have a substituent, a nitro group, a substituted hydroxycarbonylamino group, or a saturated aliphatic acylamino group or an aromatic acylamino group; X^7 and X^8 are the same or different from each other, and represent a hydrogen atom, an alkyl group, a nitro group, an amino or N-substituted amino group which may be protected by a protective group, a carboxyl group which may be protected by a protective group, a hydroxymethyl group which may be protected by a protective group, or an isocyanato group;

(i) when X^5 is a carbamoyl group which may have a substituent, X^6 represents a carboxyl group, a substituted hydroxycarbonyl group, an amino group or N-substituted amino group which may be protected by a protective group, or a nitro group;

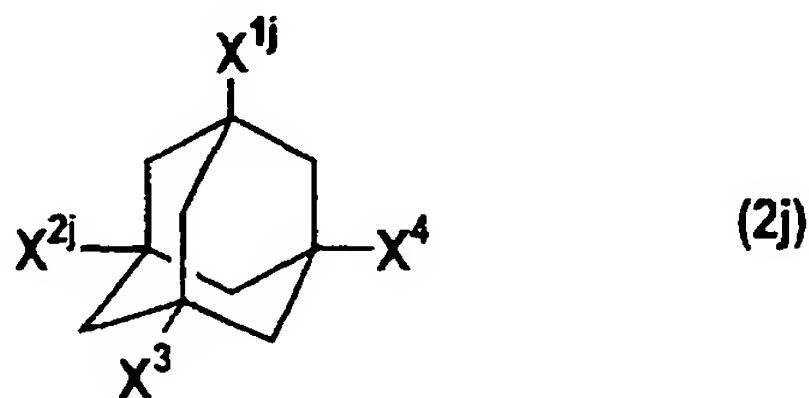
(ii) when X^5 is a nitro group, X^6 represents a substituted hydroxycarbonyl group;

(iii) when X^5 is a substituted hydroxycarbonylamino group, X^6 represents a substituted hydroxycarbonyl group, a hydroxymethyl group which may be protected by a protective group, or an amino group which may be protected by a protective group; and

(iv) X^5 is a saturated aliphatic acylamino group or an aromatic acylamino group, X^6 represents a carboxyl group, a hydroxymethyl group which may be protected by a protective group, or an amino group which may be substituted by an alkyl group;

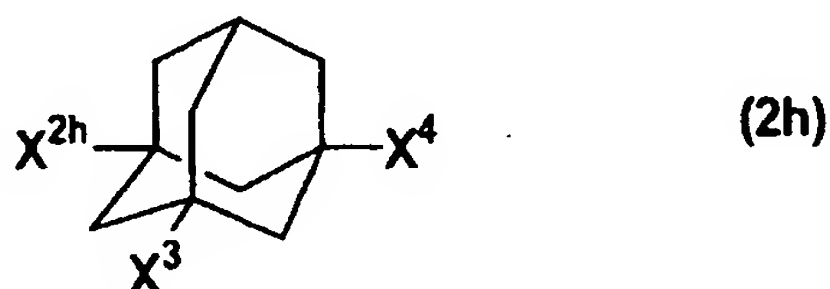
or a salt thereof.

[0025] The present invention provides a process for producing a diaminoadamantane derivative shown by the following formula (2j):

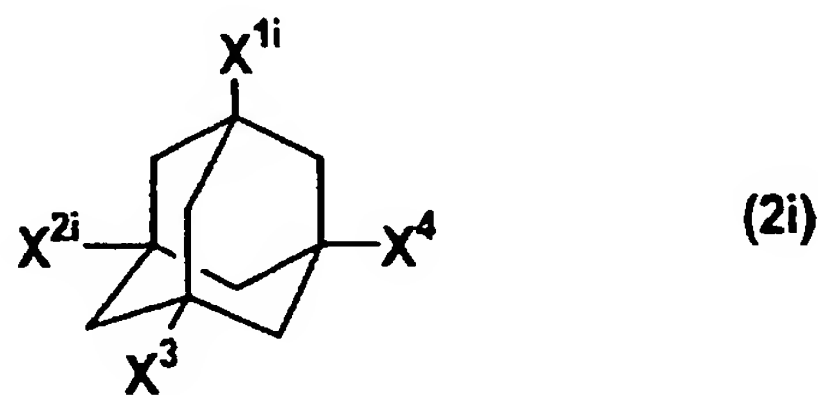


wherein X^{1j} and X^{2j} represent an amino group or N-substituted amino group which may be protected by a protective group; and X^3 and X^4 have the same meanings as defined above; which comprises steps of

contacting a compound shown by the following formula (2h):



wherein X^{2h} represents a hydrogen atom or a nitro group; X^3 and X^4 have the same meanings as defined above; with a nitrogen oxide in the presence of the imide compound shown by the formula (1), to produce a dinitroadamantane derivative shown by the following formula (2i):

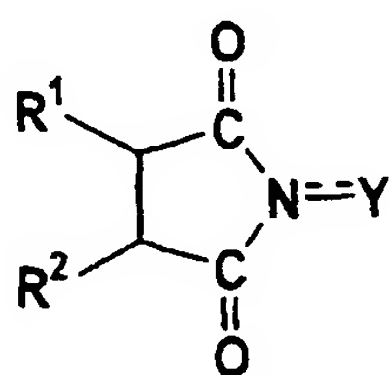


wherein X^{1i} and X^{2i} each represents a nitro group; and X^3 and X^4 have the same meanings as defined above; and reducing said dinitroadamantane derivative shown by the formula (2i) to produce a corresponding diamino compound.

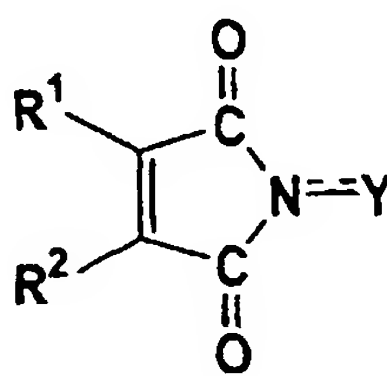
BEST MODE FOR CARRYING OUT THE INVENTION

[Imide compound]

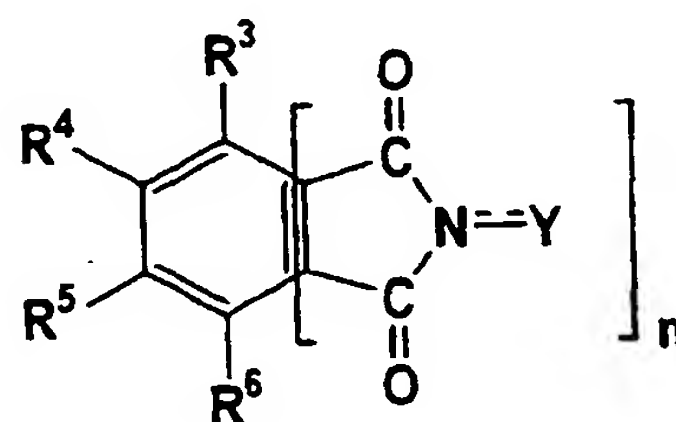
- 5 [0026] In the compound shown by the formula (1), the halogen atom, as the substituents R^1 and R^2 , includes iodine, bromine, chlorine and fluorine atoms. The alkyl group includes, for example, a straight chain or branched chain alkyl group having about 1 to 10 carbon atoms such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, t-butyl, pentyl, hexyl, heptyl, octyl, and decyl group. An illustrative preferred alkyl group includes alkyl groups having about 1 to 6 carbon atoms, in particular lower alkyl groups having about 1 to 4 carbon atoms.
- 10 [0027] As the aryl group, there may be mentioned, for instance, a phenyl group and a naphthyl group. Examples of the cycloalkyl group include cyclopentyl, cyclohexyl, and cyclooctyl groups. The alkoxy group includes, for example, an alkoxy group having about 1 to 10 carbon atoms such as methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, t-butoxy, pentyloxy, and hexyloxy group. Among them, alkoxy groups having about 1 to 6 carbon atoms, in particular lower alkoxy groups having about 1 to 4 carbon atoms are preferable.
- 15 [0028] Examples of the alkoxycarbonyl group include an alkoxycarbonyl group having about 1 to 10 carbon atoms in the alkoxy moiety such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl, isobutoxycarbonyl, t-butoxycarbonyl, pentyloxycarbonyl, and hexyloxycarbonyl group. A preferred alkoxycarbonyl group includes those each having about 1 to 6 carbon atoms in the alkoxy moiety, in particular lower alkoxycarbonyl groups each having about 1 to 4 carbon atoms in the alkoxy moiety.
- 20 [0029] The acyl group includes, for instance, an acyl group having about 1 to 6 carbon atoms such as formyl, acetyl, propionyl, butyryl, isobutyryl, valeryl, isovaleryl, and pivaloyl group.
- [0030] The substituents R^1 and R^2 may be either the same or different from each other. In the formula (1), R^1 and R^2 may bond together to form a double bond, or an aromatic or non-aromatic ring. A preferred aromatic or non-aromatic ring may be a ring having about 5 to 12 members, in particular about 6 to 10 members. Such a ring may be a hetero-
- 25 cyclic ring or a condensed heterocyclic ring, and it may practically be a hydrocarbon ring. As such a ring, there may be mentioned, for instance, non-aromatic alicyclic rings (e.g., cycloalkane rings which may have a substituent, such as cyclohexane ring, and a cycloalkene rings which may have a substituent, such as a cyclohexene ring), non-aromatic bridged (cross-linked) rings (e.g., bridged hydrocarbon rings which may have a substituent, such as a 5-norbornene ring), aromatic rings which may have a substituent, such as a benzene ring, a naphthalene ring. The ring may practically
- 30 comprise an aromatic ring.
- [0031] A preferred imide compound includes compounds shown by the following formula:



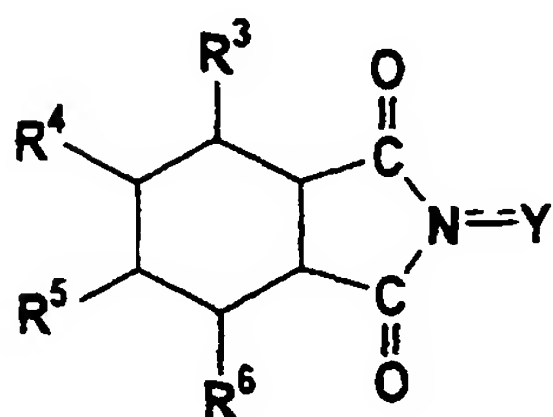
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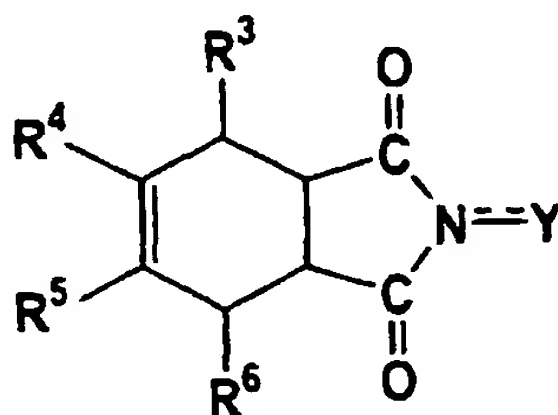
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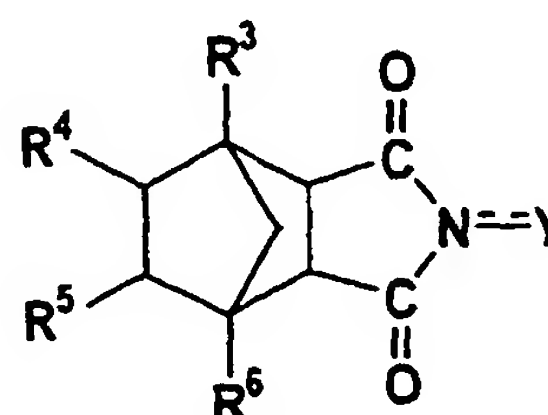
(1c)



(1d)



(1e)



(1f)

wherein R^3 , R^4 , R^5 and R^6 independently represent a hydrogen atom, an alkyl group, a hydroxyl group, an alkoxy group, a carboxyl group, an alkoxycarbonyl group, an acyl group, a nitro group, a cyano group, an amino group or a hal-

ogen atom; and R^1 , R^2 , Y and n have the same meanings as defined above.

[0032] In the substituents R^3 , R^4 , R^5 and R^6 , the alkyl group includes alkyl groups similar to those exemplified above, in particular alkyl groups each having about 1 to 6 carbon atoms. The alkoxy group includes the same alkoxy groups as mentioned above, in particular lower alkoxy groups each having about 1 to 4 carbon atoms. Examples of the alkoxycarbonyl group include the same alkoxycarbonyl groups as exemplified above, in especial lower alkoxycarbonyl groups each having about 1 to 4 carbon atoms in the alkoxy moiety. As the acyl group, there may be mentioned the similar acyl groups to those mentioned above, in particular acyl groups each having about 1 to 6 carbon atoms. Examples of the halogen atom include fluorine, chlorine and bromine atoms. The substituents R^3 , R^4 , R^5 and R^6 may practically be hydrogen atoms, lower alkyl groups each having 1 to 4 carbon atoms, carboxyl groups, nitro groups or halogen atoms, respectively.

[0033] The symbol Y in the formula (1) denotes an oxygen atom or a hydroxyl group, and n usually denotes about 1 to 3, preferably 1 or 2. The compound shown by the formula (1) can be used singly or in combination of two or more in the nitration reaction.

[0034] As examples of the acid anhydride corresponding to the imide compound of the formula (1), there may be mentioned a saturated or unsaturated aliphatic dicarboxylic acid anhydride such as succinic anhydride, maleic anhydride; a saturated or unsaturated nonaromatic cyclic polycarboxylic acid anhydride (an alicyclic polycarboxylic acid anhydride), such as tetrahydrophthalic anhydride, hexahydrophthalic anhydride (1,2-cyclohexanedicarboxylic acid anhydride), 1,2,3,4-cyclohexanetetracarboxylic acid 1,2-anhydride; a bridged cyclic polycarboxylic acid anhydride (an alicyclic polycarboxylic acid anhydride) such as hetic anhydride, himic anhydride; an aromatic polycarboxylic acid anhydride such as phthalic anhydride, tetrabromophthalic anhydride, tetrachlorophthalic anhydride, nitrophthalic anhydride, trimellitic anhydride, methylcyclohexenetetracarboxylic anhydride, pyromellitic anhydride, mellitic anhydride, 1,8;4,5-naphthalene-tetracarboxylic acid dianhydride.

[0035] Examples of a preferred imide compound include N-hydroxysuccinimide, N-hydroxymaleimide, N-hydroxyhexahydrophthalimide, N,N'-dihydroxycyclohexanetetracarboximide, N-hydroxyphthalimide, N-hydroxytetrabromophthalimide, N-hydroxytetrachlorophthalimide, N-hydroxyhetimide, N-hydroxyhimimide, N-hydroxytrimellitimide, N,N'-dihydroxypyromellitimide, N,N'-dihydroxynaphthalenetetracarboximide and so forth. A typically preferable imide compound includes an N-hydroxyimide compound derived from an alicyclic polycarboxylic acid anhydride, in particular from an aromatic polycarboxylic acid anhydride, such as N-hydroxyphthalimide.

[0036] The imide compound may be prepared by a conventional imidation process (a process for the formation of an imide), such as a process that comprises the steps of allowing a corresponding acid anhydride to react with hydroxylamine NH_2OH for ring-opening of an acid anhydride group, and closing the ring to form the imide.

[Co-catalyst]

[0037] A catalyst may comprise the imide compounds of the formula (1) and a co-catalyst. The co-catalyst includes or comprises metal compounds such as a compound comprising or containing a Group 2A element of the Periodic Table of Elements (e.g., magnesium, calcium, strontium, barium), a transition metal compound, or compounds containing a Group 3B element (e.g., boron B, aluminium Al) of the Periodic Table of Elements. These co-catalysts may be employed independently or in combination of two or more.

[0038] As the elements of the transition metal, there may be mentioned, for instance, Group 3A elements of the Periodic Table of Elements (e.g., scandium Sc, yttrium Y, and a lanthanoid element such as lanthanum La, cerium Ce, samarium Sm, an actinoid element such as actinium Ac), Group 4A elements of the Periodic Table of Elements (e.g., titanium Ti, zirconium Zr, hafnium Hf), Group 5A elements (e.g., vanadium V, niobium Nb, tantalum Ta), Group 6A elements (e.g., chromium Cr, molybdenum Mo, tungsten W), Group 7A elements (e.g., manganese Mn, technetium Tc, rhenium Re), Group 8 elements (e.g., iron Fe, ruthenium Ru, osmium Os, cobalt Co, rhodium Rh, iridium Ir, nickel Ni, palladium Pd, platinum Pt), Group 1B elements (e.g., copper Cu, silver Ag, gold Au) and Group 2B elements (e.g., zinc Zn, cadmium Cd) of the Periodic Table of Elements.

[0039] A preferred element constituting the co-catalyst includes elements of the transition metals, for example, Group 3A elements of the Periodic Table of Elements such as lanthanoid elements (e.g., Ce), actinoid elements; Group 4A elements such as Ti, Zr; Group 5A elements such as V, Nb; Group 6A elements such as Cr, Mo, W; Group 7A elements such as Mn, Tc, Re; Group 8 elements such as Fe, Ru, Co, Rh, Ni; or Group 1B elements such as Cu) and Group 3B elements such as B. The oxidation number of the metal elements constituting the co-catalyst is not particularly limited, and may be, for example 0, +2, +3, +4, +5 and +6 according to the variety of elements. The divalent transition metal compounds (such as a divalent cobalt compound, a divalent manganese compound) may be practically used as the co-catalyst.

[0040] The co-catalyst may be a simple substance or hydroxide of a metal. The co-catalyst may practically be an a metal oxide (comprising a double oxide or an oxygen acid or a salt thereof) comprising the element, an organic acid salt comprising the element, an inorganic acid salt comprising the element, a halide comprising the element, a coordinate

compound (a complex) comprising the metal element, or a polyacid (a heteropolyacid or an isopolyacid) comprising the element or a salt thereof.

[0041] As the boron compound, there may be mentioned, for example, a boron hydride (e.g., borane, diborane, tetraborane, pentaborane, decaborane); a boric acid (e.g., orthoboric acid, metaboric acid, tetraboric acid); a borate (e.g., a nickel borate, magnesium borate, manganese borate); boron oxides such as B_2O_3 ; nitrogen-containing boron compounds such as borazane, borazene, borazine, boron amide, boron imide; halides such as BF_3 , BCl_3 , tetrafluoroborate; esters of boric acid (e.g., methyl borate, phenyl borate). A preferred boron compound includes boron hydrides and boric acids such as orthoboric acid or salts thereof, in particular a boric acid.

[0042] The hydroxide includes $Mn(OH)_2$, $MnO(OH)$, $Fe(OH)_2$ and $Fe(OH)_3$, typically speaking. Examples of the metallic oxide include Sm_2O_3 , TiO_2 , ZrO_2 , V_2O_3 , V_2O_5 , CrO , Cr_2O_3 , MoO_3 , MnO , Mn_3O_4 , Mn_2O_3 , MnO_2 , Mn_2O_7 , FeO , Fe_2O_3 , Fe_3O_4 , RuO_2 , RuO_4 , CoO , CoO_2 , Co_2O_3 , RhO_2 , Rh_2O_3 , Cu_2O_3 . As examples of the double oxide or oxygen acid salt, there may be mentioned $MnAl_2O_4$, $MnTiO_3$, $LaMnO_3$, $K_2Mn_2O_5$, $CaO \cdot xMnO_2$ ($x=0.5, 1, 2, 3, 5$), manganese salts [e.g., manganates(V) such as Na_3MnO_4 , $Ba_3(MnO_4)_2$; manganates(VI) such as K_2MnO_4 , Na_2MnO_4 , $BaMnO_4$; permanganates such as $KMnO_4$, $NaMnO_4$, $LiMnO_4$, NH_4MnO_4 , $CsMnO_4$, $AgMnO_4$, $Ca(MnO_4)_2$, $Zn(MnO_4)_2$, $Ba(MnO_4)_2$, $Mg(MnO_4)_3$, $Cd(MnO_4)_2$].

[0043] As the organic acid salts, there may be exemplified as salts of a C_{2-20} fatty acid such as cobalt acetate, manganese acetate, cobalt propionate, manganese propionate, cobalt naphthenate, manganese naphthenate, cobalt stearate and manganese stearate, and manganese thiocyanate and corresponding salts of Ce, Ti, Zr, V, Cr, Mo, Fe, Ru, Ni, Pd, Cu and Zn. The inorganic acid salt includes, for instance, nitrates such as cobalt nitrate, iron nitrate, manganese nitrate, nickel nitrate and copper nitrate, and sulfates, phosphates and carbonates each corresponding to these nitrates (e.g., cobalt sulfate, iron sulfate, manganese sulfate, cobalt phosphate, iron phosphate, manganese phosphate, an iron carbonate, a manganese carbonate, iron perchlorate). As the halides, there may be mentioned, for instance, chlorides such as $SmCl_3$, $SmCl_2$, $TiCl_2$, $ZrCl_2$, $ZrOCl_2$, VCl_3 , $VOCl_2$, $MnCl_2$, $MnCl_3$, $FeCl_2$, $FeCl_3$, $RuCl_3$, $CoCl_3$, $RhCl_2$, $RhCl_3$, $NiCl_2$, $PdCl_2$, $PtCl_2$, $CuCl$ and $CuCl_2$, or halides such as fluorides, bromides or iodides each corresponding to these chlorides (e.g., MnF_2 , $MnBr_2$, MnF_3 , FeF_2 , FeF_3 , $FeBr_2$, $FeBr_3$, FeI_2 , $CuBr$, $CuBr_2$), complex halides such as M^1MnCl_3 , $M^1_2MnCl_4$, $M^1_2MnCl_5$, $M^1_2MnCl_6$, wherein M^1 represents a monovalent metal.

[0044] The ligand constituting the complex includes, for example, OH (hydroxo); alkoxy groups such as methoxy, ethoxy, propoxy and butoxy group; acyl groups such as acetyl (OAc), propionyl group; alkoxycarbonyl groups such as methoxycarbonyl (acetato), ethoxycarbonyl group; acetylacetonato (AA), cyclopentadienyl group; halogen atoms such as chlorine, bromine; CO, CN, oxygen atom, H_2O (aquo); phosphorus compounds such as a phosphine (e.g., triphenylphosphine and other triarylphosphine); nitrogen-containing compounds such as NH_3 (ammine), NO, NO_2 (nitro), NO_3 (nitrate), ethylenediamine, diethylenetriamine, pyridine and phenanthroline. In the complexes or complex salts, the same or different ligands may be coordinated singly or in combination of two or more. The preferable ligand includes, for example, OH, an alkoxy group, an acyl group, an alkoxycarbonyl group, acetylacetonato, a halogen atom, CO, CN, H_2O (aquo), triphenylphosphine and other phosphorus compounds, and a nitrogen-containing compound inclusive of NH_3 , NO_2 and NO_3 .

[0045] A preferable complex includes the complexes containing the preferable transition metal element. The transition metal element and the ligand may optionally be employed in combination to form a complex. Such a complex includes, for instance, acetylacetonato complexes [e.g., acetylacetonato complex of Ce, Sm, Ti, Zr, V, Cr, Mo, Mn, Fe, Ru, Co, Ni, Cu and Zn, titanylacetylacetonato complex $TiO(AA)_2$, zirconylacetylacetonato complex $ZrO(AA)_2$, vanadylacetylacetonato complex $VO(AA)_2$], cyano complexes [e.g., a hexacyanomanganate(II), a hexacyanoferrate(II)], carbonyl complexes or cyclopentadienyl complexes [e.g., tricarbonylcyclopentadienylmanganese(I), biscyclopentadienylmanganese(II), biscyclopentadienyliron(II), $Fe(CO)_5$, $Fe_2(CO)_9$, $Fe_3(CO)_{12}$], nitrosyl compounds [e.g., $Fe(NO)_4$, $Fe(CO)_2(NO)_2$], thiocyanato complexes [e.g., thiocyanatocobalt, thiocyanatomanganese, thiocyanatoiron], or acetyl complexes [e.g. cobalt acetate, manganese acetate, iron acetate, copper acetate, zirconyl acetate $ZrO(OAc)_2$, titanyl acetate $TiO(OAc)_2$, vanadyl acetate $VO(OAc)_2$].

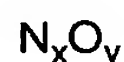
[0046] The polyacid is practically at least one member selected from Group 5 elements or Group 6 elements of the Periodic Table of Elements, such as V (vanadic acid), Mo (molybdic acid) and W (tungstic acid), typically speaking. There is no particular limit as to the central atom, and it may be any of, for instance, Be, B, Al, Si, Ge, Sn, Ti, Zr, Th, N, P, As, Sb, V, Nb, Ta, Cr, Mo, W, S, Se, Te, Mn, I, Fe, Co, Ni, Rh, Os, Ir, Pt or Cu. As illustrative examples of the heteropolyacid, there may be mentioned cobaltmolybdic acid, cobalttungstic acid, molybdenumtungstic acid, manganesemolybdic acid, manganesetungstic acid, manganesemolybdenumtungstic acid, vanadomolybdophosphoric acid, manganesevanadiummolybdic acid, manganesevanadomolybdophosphoric acid, vanadiummolybdic acid, vanadiumtungstic acid, silicomolybdic acid, silicotungstic acid, phosphomolybdic acid, phosphotungstic acid, phosphovanadomolybdic acid, and phosphovanadotungstic acid.

[0047] The catalysts have high activities. A combination of the catalyst with at least one reactant selected from (i) a nitrogen oxide and (ii) a mixture of carbon monoxide and oxygen, accelerates a nitration and/or carboxylation reaction of a substrate even in a mild or moderate condition.

[0048] A catalyst comprising the imide compound shown by the formula (1) or the imide compound and the above co-catalyst may be whichever of a homogeneous system or a heterogeneous system. The catalyst may be a solid catalyst comprising a catalytic component supported on a support or carrier, as well. As the support, use can be practically made of porous supports such as active carbon, zeolite, silica, silica-alumina, and bentonite. In the solid catalyst, the supporting amount of the imide compound of the formula (1) as the catalyst component may be about 0.1 to 50 parts by weight, preferably about 0.5 to 30 parts by weight and more preferably about 1 to 20 parts by weight relative to 100 parts by weight of the support. The supporting amount more of the co-catalyst is about 0.1 to 30 parts by weight, preferably about 0.5 to 25 parts by weight, and more preferably about 1 to 20 parts by weight, relative to 100 parts by weight of the support.

[Nitrogen oxide]

[0049] The nitrogen oxide may be shown by the formula:



wherein x denotes an integer of 1 or 2 and y denotes an integer of 1 to 6.

[0050] In the compound shown by the above formula, when x is 1, y is usually an integer of 1 to 3; and when x is 2, y is usually an integer of 1 to 6.

[0051] Such nitrogen oxide may be exemplified N_2O , NO, N_2O_3 , NO_2 , N_2O_4 , N_2O_5 , NO_3 and N_2O_6 . These nitrogen oxides may be used independently or in combination.

[0052] The preferred nitrogen oxide includes (i) a nitrogen oxide (particularly N_2O_3) generated by the reaction of at least one nitrogen oxide selected from dinitrogen oxide (N_2O) and nitrogen monoxide (NO) with oxygen, or a nitrogen oxide containing N_2O_3 as a main component and (ii) a nitrogen dioxide (NO_2) or a nitrogen oxide containing NO_2 as a main component.

[0053] Nitrogen oxide N_2O_3 may be easily obtained by a reaction of N_2O and/or NO with oxygen. To be more concrete, the nitrogen oxide may be prepared by introducing nitrogen monoxide and oxygen to a reactor to produce a blue liquid N_2O_3 . Therefore, the nitration reaction may be carried out by introducing N_2O and/or NO and oxygen to a reaction system without producing N_2O_3 in advance.

[0054] Incidentally, a pure oxygen may be used or may be distilled by an inert gas (e.g., carbon dioxide, nitrogen, helium and argon). Air may be used as an oxygen source.

[Mixture of carbon monoxide and oxygen]

[0055] Carbon monoxide or oxygen employed in the present invention may be pure one, and may be diluted with a inert gas (e.g., nitrogen, helium, argon, carbon dioxide). The oxygen source may be air. To the reaction system, a mixture previously mixed carbon monoxide with oxygen may be introduced, and carbon monoxide and oxygen may separately introduced.

[0056] In the present invention, as a reactant, there may be employed, for example, (i) the nitrogen oxide, (ii) the mixture of carbon monoxide and oxygen, or a combination of (i) the nitrogen oxide and (ii) the mixture of carbon monoxide and oxygen. In the case of using (i) the nitrogen oxide as a reactant, a substrate is nitrated to generate a nitro compound. In the case of using (ii) the mixture of the nitrogen monoxide and oxygen as the reactant, a substrate is carboxylated to generate a carboxyl compound. In the case of using (i) the nitrogen monoxide and (ii) the mixture of carbon monoxide and oxygen in combination as the reactant, a nitro compound and a carboxyl compound can be co-produced. In this case, use of a compound having plural reactive sites as a substrate can provide a compound which has a nitro group and a carboxyl group in the same molecule in one step by selecting a reaction condition (e.g., the ratio of the reactant (i) to (ii), a reaction temperature).

[Substrate]

[0057] Species of substrates is not particularly restricted, and may be employed broad range of a saturated or unsaturated compound such as a hydrocarbon (e.g., an aliphatic hydrocarbon, an alicyclic hydrocarbon, an aromatic hydrocarbon), a heterocyclic compound, an alcohol, an ether, a ketone, an aldehyde, a carboxylic acid or derivative thereof, and the like may be employed.

[0058] Preferred substrate comprises, for example, (a) a compound having a methyl group or a methylene group at the adjacent site of an unsaturated bond, (b) a homo- or heterocyclic compound having a methylene group, (c) a compound having a methine carbon atom, (d) a compound having a methyl group or a methylene group at the adjacent site of an aromatic ring and (e) a compound having a methyl group or a methylene group at the adjacent site of a carbonyl

group. In the compound (b), the methylene group constitutes a 5- or 6-membered ring, and the compound (b) is usually a non-aromatic homo- or heterocyclic compound.

(a) The compound having a methyl group or a methylene group at the adjacent site of an unsaturated bond comprises an organic compound having a double bond and/or a triple bond. Examples of such compounds include propylene, 1-butene, 2-butene, butadiene, 1-pentene, 2-pentene, isoprene, 2-methyl-2-butene, 1-hexene, 2-hexene, 1,5-hexadiene, 2,3-dimethyl-2-butene, 3-hexene, 1-heptene, 2-heptene, 1,6-heptadiene, 1-octene, 2-octene, 3-octene, 1,7-octadiene, 2,6-octadiene, 1-nonene, 2-nonene, decene, decadiene, dodecadiene, dodecatriene, undecene, undecadiene and undecatriene.

(b) Examples of the homocyclic compound (b1) having methylene group include a cycloalkane (e.g., a cycloalkane having about 3 to 30 carbon atoms such as cyclopropane, cyclobutane, cyclopentane, cyclohexane, cycloheptane, methylcyclohexane, cyclooctane, 1,2-dimethylcyclohexane, cyclononane, isopropylcyclohexane, methylcyclooctane, cyclodecane, cyclododecane, cyclotridecane, cyclotetradecane, cyclopentadecane, cyclohexadecane, cyclooctadecane, cyclononadecane), a cycloalkene (e.g., a cycloalkene having about 3 to 30 carbon atoms such as cyclopropene, cyclobutene, cyclopentene, cyclohexene, cycloheptene, 1-methyl-1-cyclohexene, cyclooctene, cyclononene, cyclodecene, cyclododecene, limonene, menthene, menthone), a cycloalkadiene (e.g., a cycloalkadiene having about 5 to 30 carbon atoms such as cyclopentadiene, cyclohexadiene, cycloheptadiene, cyclooctadiene, cyclodecadiene, cyclododecadiene), a cycloalkatriene (e.g., cyclooctatriene), cycloalkatetraene (e.g., cyclooctatetraene) and a condensed polycyclic hydrocarbon.

(b) The heterocyclic compound (b2) having a methylene group comprises a 5- or 6-membered cyclic compound having at least one hetero atom selected from nitrogen atom, oxygen atom and sulfur atom, or a condensed heterocyclic compound which is condensed by the 5- or 6-membered cyclic compound having the hetero atom at an aromatic ring, such as dihydrofuran, tetrahydrofuran, pyran, dihydropyran, tetrahydropyran, piperidine, piperadine, pyrrolidine, xanthene, and the like.

(c) The compound having a methine carbon atom (methyldine group) comprises, for instance, a chain hydrocarbon (c1) having a tertiary carbon atom, a bridged cyclic hydrocarbon (c2) and the like.

Examples of the chain hydrocarbon (c1) having a tertiary carbon atom include an aliphatic hydrocarbon having about 4 to 10 carbon atoms such as isobutane, isopentane, isohexane, 3-methylpentane, 2,3-dimethylbutane, 2-methylhexane, 3-methylhexane, 2,3-dimethylpentane, 2,4-dimethylpentane, 2,3,4-trimethylpentane, 3-ethylpentane, 2,3-dimethylhexane, 2,4-dimethylhexane, 3,4-dimethylhexane, 2,5-dimethylhexane, 2-propylhexane, 2-methylheptane, 4-methylheptane, 2-ethylheptane, 3-ethylheptane, 2,6-dimethylheptane, 2-methyloctane, 3-methyloctane, 2,7-dimethyloctane and 2-methylnonane.

The bridged cyclic hydrocarbon (c2) comprises, for example, a bridged cyclic hydrocarbon [e.g., bicyclo hydrocarbon such as decalin, hexahydroindan, carane, bornane, norbornene, norbornane, vinylnorbornene and norbornadiene; a tricyclo hydrocarbon such as homoblendane, adamantane and derivatives thereof (e.g., methyladamantane, 1,3-dimethyladamantane, ethyladamantane, chloroadamantane, adamantanol, adamantanone, methyladamantanone, dimethyladamantanone, formyladamantanone), tricyclo[4.3.1.^{1,2,5}]undecane; and a tetracyclohydrocarbon such as tetracyclo[4.4.0.1.^{2,5}.1.^{7,10}]dodecane], a dimer of a diene or hydrogen adduct thereof (e.g., dicyclopentane, dicyclohexane, dicyclopentene, dicyclohexadiene, dicyclopentadiene, tetrahydrodicyclopentadiene) and a terpene (e.g., pinane, pinene, camphor, bornene, caryophyllene).

The preferred compound (c) having a methine carbon atom includes a bridged cyclic hydrocarbon having about 6 to 16 carbon atoms, in particular about 7 to 14 (especially a bridged cyclic hydrocarbon such as adamantane or a derivative thereof).

(d) Examples of the compound having a methyl group or a methylene group at the adjacent site of an aromatic ring include an aromatic hydrocarbon having an alkyl group (e.g., toluene, o-, m- or p-xylene, 1,2,3-trimethylbenzene, 1,2,4-trimethylbenzene, 1,3,5-trimethylbenzene (mesitylene), 1,2,3,4-tetramethylbenzene, 1,2,3,5-tetramethylbenzene, 1,2,4,5-tetramethylbenzene (durene), 1,2,3,4,5,6-hexamethylbenzene, ethylbenzene, propylbenzene, cumene, o-, m- or p-ethyltoluene, butylbenzene, 1,4-diethylbenzene, 1-methylnaphthalene, 2-methylnaphthalene, 1,5-dimethylnaphthalene, 2,5-dimethylnaphthalene, 1-methylantracene, 2-methylantracene, 9-methylantracene, dimethylantracene, trimethylantracene, 4,4'-dimethylbiphenyl, dibenzyl, diphenylmethane, triphenylmethane), an aromatic hydrocarbon having a cyclic methylene group (e.g., a condensed polycyclic aromatic hydrocarbon condensed by a about 5 to 8-membered ring, such as indane, indene, tetralin, dihydronaphthalene, fluorene, phenalene) and a heterocyclic compound having an alkyl group (e.g., a picoline such as 2-methylfuran, 3-methylfuran, 2-methylpyran, 3-methylpyran, 4-methylpyran, 3,4-dimethylpyran, 4-methylchroman, 6-methylchroman, 2-methylpyridine, 3-methylpyridine and 4-methylpyridine, a lutidine such as 2,3-dimethylpyridine, a collidine such as 2,4,6-trimethylpyridine, 2-ethylpyridine, 3-ethylpyridine, 4-ethylpyridine, methylquinoline and methylindole). The preferred compound (d) includes a compound having a methyl group or a methylene group at benzyl position.

(e) The compound having a (active) methyl group or methylene group at the adjacent site of a carbonyl group com-

prises, for instance, an aldehyde (e1), a ketone (e2) and a carboxylic acid or derivative thereof (e3).

[0059] The aldehyde (e1) comprises, for example, an aliphatic aldehyde (e.g., an aliphatic monoaldehyde having about 2 to 12 carbon atoms such as acetaldehyde, propionaldehyde, butylaldehyde, isobutylaldehyde, pentylaldehyde, hexylaldehyde, heptylaldehyde, octylaldehyde, nonylaldehyde and decylaldehyde, an aliphatic polyaldehyde such as malonaldehyde, succinaldehyde, adipic aldehyde and sebacic aldehyde), an aromatic aldehyde (e.g., benzaldehyde, anisaldehyde), an alicyclic aldehyde (e.g., formylcyclohexane, citronellal), a bridged cyclic aldehyde (e.g., formylnorbornene) and a heterocyclic aldehyde (e.g., nicotinic aldehyde, furfural).

[0060] Examples of the ketone (e2) include an aliphatic ketone (e.g., acetone, methylethylketone, methylisopropylketone, methylisobutylketone, methyl-t-butylketone, 2-pentanone, 3-pentanone, 2-hexanone, 3-hexanone, 2-heptanone, 3-heptanone, 4-heptanone, 2-octanone, 3-octanone, 4-octanone, 2-nonanone and 2-decanone), a cyclic ketone (e.g., a non-aromatic cyclic mono- or polyketone such as cyclopentanone, cyclohexanone, methylcyclohexanone, dimethylcyclohexanone, cycloheptanone, isophorone, cyclooctanone, cyclononanone, cyclodecanone, cyclohexadione and cyclooctadione; a cyclic ketone having an aromatic ring such as α -tetralone, β -tetralone and indanone), a bridged cyclic ketone (e.g., pinocampnone, pinocarbon), an aromatic ketone (e.g., acetophenene, propiophenone) and a heterocyclic ketone (e.g., pyrrolidone, piperidone).

[0061] The carboxylic acid or derivatives thereof (e3) comprises, for example, an aliphatic dicarboxylic acid or derivatives thereof (e.g., malonic acid or an ester thereof, succinic acid or an ester thereof and glutaric acid or an ester thereof).

[0062] These substrates may be substituted by a suitable functional group, such as a halogen atom, an oxo group, a hydroxyl group, an alkoxy group, a carboxyl group, an alkoxy carbonyl group, an acyl group, an alkyl group, an alkenyl group (e.g., an allyl group), a cycloalkyl group, an aryl group, a vinyl group, an amino group, an alkylamino group, an amido group, a nitro group, a nitrile group, an acylamino group, a mercapto group, a sulfonyl group, a sulfinyl group, a sulfide group and a phosphino group.

[0063] In such substrates (a), (b), (c), (d) and (e), a nitro group or a carboxyl group can be introduced thereto at a carbon atom of a methyl or methylene group, or a methine carbon atom. To be specific, a nitro group or a carboxyl group can be smoothly introduced to the compound (c) at a methine carbon atom such as a cyclic methine carbon atom of the bridged cyclic hydrocarbon to provide a nitro compound or a carboxy compound of the bridged cyclic hydrocarbons with the high conversion and selectivity. Contact of, for example, adamantane among the bridged cyclic hydrocarbons with the nitrogen oxide in the presence of the catalyst provides 1-nitroadamantane and/or 1,3-dinitroadamantane and/or 1,3,5-trinitroadamantane etc. Contact of adamantane with carbon monoxide and oxygen provides 1-carboxyadamantane and/or 1,3-dicarboxyadamantane and/or 1,3,5-tricarboxyadamantane etc. Moreover, contact of adamantane with the nitrogen oxide, carbon monoxide and oxygen in the presence of the catalyst provides 1-carboxy-3-nitroadamantane, 1-carboxy-3,5-dinitroadamantane, 1,3-dicarboxy-5-nitroadamantane etc. Furthermore, contact of 1-methyladamantane with the nitrogen oxide provides 1-methyl-3-nitroadamantane, contact of 1-methyladamantane with carbon monoxide and oxygen provides 1-carboxy-3-methyladamantane etc.

[0064] In (d) the compound having a methyl group or a methylene group at an adjacent site of an aromatic ring, a nitro group or a carboxyl group can be smoothly introduced thereto at the benzyl position. Contact of, for example, toluene among the compound having a methyl group or a methylene group at the benzyl position with the nitrogen oxide in the presence of the catalyst provides nitrobenzene etc. and contact of toluene with the carbon monoxide and oxygen provides phenylacetate. Use of ethylbenzene as a substrate provides 1-nitroethylbenzene, 1-phenylpropionate etc. Application of the process of the present invention to fluorene provides 9-carboxyfluorene.

[Amount and ratio of the each component]

[0065] The amount of the imide compound shown by the formula (1) may be selected within a broad range, for example, of about 0.0001 mole (0.01 mole%) to 1 mole (100 mole%), preferably about 0.001 mole (0.1 mole%) to 0.5 mole (50 mole%), more preferably about 0.01 to 0.30 mole, and may be practically about 0.01 to 0.25 mole, relative to 1 mole of the substrate.

[0066] The amount of the co-catalyst may be selected within a broad range of, for example, about 0.0001 mole (0.01 mole%) to 0.7 mole (70 mole%), preferably about 0.0001 mole to 0.5 mole, more preferably about 0.001 to 0.3 mole, and may be practically about 0.0005 to 0.1 mole (e.g., about 0.005 to 0.1 mole), relative to 1 mole of the substrate.

[0067] The ratio of the co-catalyst to the imide compound shown by the formula (1) may be selected within the range not interfering with the reaction rate or selectivity, for example, of about 0.001 to 10 mole of the co-catalyst, preferably about 0.005 to 5 mole, more preferably about 0.01 to 3 mole, and may be practically about 0.01 to 5 mole, relative to 1 mole of the imide compound.

[0068] The amount of the nitrogen oxide may be selected depending upon the introduced amount of nitro group, within the range of, for example, about 1 mole or more (e.g., about 1 to 50 mole), preferably about 1.5 to 30 mole, and may be

usually about 2 to 25 mole, relative to 1 mole of the substrate.

[0069] The amount of carbon monoxide may be selected within the range of, for example, about 1 mole or more (e.g., about 1 to 1000 mole), preferably excess mole, for example, about 1.5 to 100 mole (e.g., about 2 to 50 mole), more preferably about 2 to 30 mole (e.g., about 5 to 25 mole), relative to 1 mole of the substrate.

5 [0070] The amount of oxygen may be selected within the range of about 0.5 mole or more (e.g., about 0.5 to 100 mole), preferably about 0.5 to 30 mole, more preferably about 0.5 to 25 mole, relative to 1 mole of the substrate.

[0071] In a continuous reaction, when excess amount of carbon monoxide and oxygen are used, they can be used to supply to the reaction system continuously by, for example, circulating them.

10 [0072] The ratio of carbon monoxide (CO) to oxygen (O₂) may be selected within the wide range, as far as the amount of the each component is within the above range, for example, of CO/O₂ = about 1/99 to 99.99/0.01 (mole%) [e.g., about 70/30 to 99/1 (mole%)]. Use of more amount of the carbon monoxide than that of oxygen is advantageous. The ratio of CO to O₂ may be usually selected within the range of CO/O₂ = about 1/99 to 99/1 (mole%) [e.g., about 10/90 to 99/1 (mole%)], and may be preferably about 30/70 to 98/2 (mole%), more preferably about 50/50 to 95/5 (mole%), particularly about 60/40 to 90/10 (mole%).

15 [0073] The volume ratio of carbon monoxide to oxygen in a supply line may be selected within the range of, for example, CO/O₂ = about 1/99 to 99.99/0.01 (volume%) [e.g., about 70/30 to 99/1 (volume%)], and may be usually about 1/99 to 99/1 (volume%), preferably about 30/70 to 98/2 (volume%), more preferably about 50/50 to 95/5 (volume%), specifically about 60/40 to 90/10.

20 [Nitration reaction and carboxylation reaction]

[0074] The nitration reaction and/or the carboxylation reaction can be conducted in the presence or absence of a solvent. As the solvent, use can be made of a solvent inert to reaction, examples of which are organic acids (e.g., carboxylic acids such as acetic acid and propionic acid), nitriles (e.g., acetonitrile, propionitrile, benzonitrile), amides (e.g., formamide, dimethylformamide), alcohols (e.g., ethanol, propanol, butanol, t-butanol, t-amylalcohol), aliphatic hydrocarbons (e.g., hexane, octane), aromatic hydrocarbons (e.g., benzene), organic halogen compounds (e.g., halogenated hydrocarbons such as dichloromethane, chloroform, dichloroethane, dichlorobenzene, and trifluoromethylbenzene; halogen-substituted carboxylic acids such as chloroacetic acid and trifluoroacetic acid; halogen-substituted acid anhydrides such as chloroacetic anhydride; halogen-substituted esters such as methyl chloroacetate and ethyl chloroacetate), nitro compounds (e.g., nitromethane, nitrobenzene), esters (e.g., ethyl acetate), ethers (e.g., dimethyl ether), and mixed solvents of these. Among them, carboxylic acids (e.g., acetic acid, propionic acid), organic halogen compounds and nitriles are preferred as the solvent. A mixture of two or more solvents serves to enhance the yield and selectivity. As the solvent mixtures, there may be mentioned a mixed solvent comprising at least one solvent selected from nitriles and organic halogen compounds (e.g., a mixed solvent of a nitrile and an organic halogen compound, a mixed solvent of a nitrile and an organic acid), and the like. When the solvents are used in combination, the ratio for blending these solvents can be selected from a wide range. For instance, the ratio of a dominant primary solvent relative to the other solvent(s) ranges from about 1/99 to 99/1 (the former/the latter, by weight), preferably from about 5/95 to 95/5 (by weight), and more preferably about 10/90 to 90/10 (by weight) (e.g., 15/85 to 85/15 (by weight)).

35 [0075] In the present invention, the reactions can be smoothly conducted even in a comparatively mild or moderate condition. The reaction temperature may be suitably selected according to species of the reactions, species of the imide compounds or the substrates. For example, in the nitration reaction, the reaction temperature may be selected within the range of about 0 to 150°C, preferably about 25 to 125°C, more preferably about 30 to 100°C. The nitration reaction smoothly proceeds at a comparatively lower temperature such as within the range about 20 to 60°C. In the carboxylation reaction, the reaction temperature may be selected within the range of about 0 to 200°C, preferably about 10 to 150°C (e.g., about 10 to 120°C), more preferably about 10 to 100°C (e.g., about 10 to 80°C). The reaction can be conducted under ambient pressure or in a pressure (under load).

[0076] When a nitrogen oxide is used as a reactant, a reaction in the presence of oxygen sometimes provides a nitroalcohol or an alcohol. The nitroalcohol is included in the nitro compound of the present invention.

50 [0077] The process of the present invention is useful for nitrating and/or carboxylating a substrate to provide a nitro compound and/or carboxyl compound corresponding to the substrate, efficiently. In the process, the compound can be obtained with high conversion and selectivity even in a mild and moderate condition. To be specific, when a mixture of carbon monoxide and oxygen is employed as a reactant a carboxyl group can be directly introduced to a substrate, and a carboxyl compound having more carbon atoms than the substrate depending on the introduced amount of carboxyl groups. Thus, in the present invention, a substrate is contacted with carbon monoxide and oxygen in the presence of the catalyst to provide a carboxyl compound at fewer reaction steps.

55 [0078] The reaction may be conducted in any of a batch, semi-batch, or continuous system. After the completion of the reaction, the reaction product can be easily separated and purified by a conventional separation/purification method including such separation methods as filtration, concentration, distillation, extraction, crystallisation, recrystallisation,

adsorption, column chromatography, and a combination of these separation methods.

[Adamantane derivative]

5 **[0079]** In the adamantane derivative shown by the formulas (2) and (3), a protective group of a hydroxymethyl group (the moiety corresponding to hydroxyl group of hydroxymethyl group) is included, for instance, t-butyl group, a cycloalkyl group (e.g., cyclohexyl group), an aralkyl group (e.g., benzyl group, 2,6-dichlorobenzyl group, 3-bromobenzyl group, 2-nitrobenzyl group, 4-dimethylcarbamoylbenzyl group, a benzyl group which may have a substituent such as triphenylmethyl group), tetrahydropyranyl group, an acyl group [e.g., a saturated
10 aliphatic acyl group [(e.g., a saturated C₂₋₆ aliphatic acyl group such as acetyl group, propionyl group, isopropionyl group, butyryl group, isobutyryl group, valeryl group, isovaleryl group, pyvaloyl group, preferably a C₂₋₄ saturated aliphatic acyl group), an aromatic acyl group (e.g., a C₇₋₁₃ aromatic acyl group such as benzoyl group, p-phenylbenzoyl, phthaloyl, naphtoyl), an alicyclic acyl group (a cycloalkyl-carbonyl group; such as cyclohexylcarbonyl)], an alkoxy carbonyl group such as a C₁₋₆alkoxy-carbonyl group (e.g., methoxy carbonyl group, ethoxy carbonyl group, propyloxy carbonyl group, isopropoxy carbonyl group, isobutyloxy carbonyl group, t-butyloxy carbonyl group), an alalkyloxy carbonyl group (e.g., benzyloxy carbonyl group, methoxybenzyloxy carbonyl group), a carbamoyl group, which may have a substituent such as a C₁₋₆alkyl group and a C₆₋₁₄aryl group, (e.g., carbamoyl group, methylcarbamoyl group, ethylcarbamoyl group, phenyl carbamoyl group), a dialkylphosphinotioyl group (e.g., dimethylphosphinotioyl group), a diarylphosphinotioyl group (e.g., diphenylphosphinotioyl group). A preferred protective group of hydroxymethyl group
20 includes, for instance, an acyl group (specifically, a saturated C₂₋₆aliphatic acyl group etc., more specifically, a saturated C₂₋₄aliphatic acyl group etc.), a C₁₋₆alkoxy-carbonyl group, a carbamoyl group which may have a substituent.

[0080] A protective group of amino group includes, for example, as illustrated in the paragraph of the protective group of the hydroxyl group, t-butyl group, an aralkyl group, a non-polymerizable acyl group [such as a saturated aliphatic acyl group (e.g., a saturated C₂₋₆aliphatic acyl group, especially, a saturated C₂₋₄aliphatic acyl group), an aromatic acyl group (e.g., a C₇₋₁₃aromatic acyl group), an alicyclic acyl group], an alkoxy carbonyl group (e.g., a C₁₋₆alkoxy carbonyl group), an aralkyloxy carbonyl group, a dialkylphosphinotioyl group, a diarylphosphinotioyl group. A preferred protective group of amino group comprises, for instance, a non-polymerizable acyl group [such as a saturated C₂₋₆aliphatic acyl group (specifically, a saturated C₂₋₄aliphatic acyl group), a C₇₋₁₃aromatic acyl group], an alkoxy carbonyl group (specifically, a C₁₋₆alkoxy carbonyl group).

30 **[0081]** An N-substituted amino group includes, for example, a mono- or di-C₁₋₆alkylamino group (e.g., methylamino group, ethylamino group, a propylamino group, dimethylamino group, diethylamino group), preferably, a mono- or di-C₁₋₄alkylamino group.

[0082] A protective group of a carboxyl group comprises, for instance, an alkoxy group such as a C₁₋₁₀alkoxy group (e.g., methoxy group, ethoxy group, propoxy group, isopropoxy group, butoxy group, isobutoxy group, s-butoxy group, t-butoxy group, hexyloxy group), preferably, a C₁₋₆alkoxy group, especially, a C₁₋₄alkoxy group, a cycloalkyloxy group (e.g., cyclohexyloxy group), an aryloxy group (e.g., phenoxy group), an aralkyloxy group (e.g., benzyloxy group, diphenylmethyloxy group), a trialkylsilyloxy group (e.g., trimethylsilyloxy group), an amino group which may have a substituent [amino group; an N-substituted amino group, such as a mono- or di-C₁₋₆ alkyl amino group (e.g., methylamino group, dimethylamino group, ethylamino group, diethylamino group)], hydrazino group, an alkoxy carbonyl hydrazino group (e.g., t-butoxycarbonylhydrazino group), an aralkyloxycarbonylhydrazino group (e.g., benzyloxycarbonylhydrazino group). A preferred protective group of carboxyl group includes an alkoxy group (especially, a C₁₋₆alkoxy group), an amino group which may have a substituent (e.g., an N-substituted amino group, especially, a mono- or di-C₁₋₆alkylamino group).

45 **[0083]** An alkyl group comprises, for instance, a C₁₋₆alkyl group, such as methyl, ethyl, propyl, isopropyl, butyl, isoutyl, s-butyl, t-butyl, hexyl, preferably, a C₁₋₄alkyl group, more preferably, methyl group or ethyl group.

[0084] In the compound shown by the formula (3), a substituent of a carbamoyl group includes, for example, a C₁₋₆alkyl group such as methyl, ethyl, propyl, butyl, and isobutyl group and a C₆₋₁₄aryl group such as phenyl and naphthyl group. A substituted hydrooxycarbonylamino group includes, for example, a C₁₋₆alkoxy-carbonylamino group such as methoxycarbonylamino, ethoxycarbonylamino, propoxycarbonylamino, and butoxycarbonylamino group; a C₆₋₁₄aryloxy-carbonylamino group such as phenyloxycarbonylamino and naphthyloxycarbonylamino group; and a C₇₋₁₅aralkyloxy-carbonylamino group such as benzyloxycarbonylamino group.

50 **[0085]** Examples of a saturated aliphatic acylamino group include a saturated C₂₋₆aliphatic acylamino group such as acetilamino, propionylamino, isopropionylamino, butylamino, isobutylamino, valerylamino, isovalerylamino, and pivaloylamino group, and preferably a saturated C₂₋₄aliphatic acylamino group. An aromatic acylamino group includes, for example, an aromatic C₇₋₁₃acylamino such as benzoylamino and naphtoylamino group. A substituted oxycarbonyl group includes, for example, a C₁₋₆alkoxy-carbonyl group such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl and butoxycarbonyl group; a C₆₋₁₄aryloxy-carbonyl group such as phenyloxycarbonyl and naphthyloxycarbonyl group; a C₇₋₁₅aralkyloxy-carbonyl group such as benzyloxycarbonyl group. An alkyl group as a substituent of an amino group

includes, for example, a C₁₋₆alkyl group such as methyl, ethyl, propyl, butyl and isobutyl group.

[0086] Examples of a preferred X¹ include nitro group, amino group, a C₂₋₆acylamino group corresponding to an amino group protected by a C₂₋₆acyl group, a C₁₋₆alkoxy-carbonylamino group corresponding to an amino group protected by a C₁₋₆alkoxy-carbonyl group, carboxyl group, a C₁₋₁₀alkoxy-carbonyl group corresponding to a carboxyl group protected by a C₁₋₁₀alkoxy group (especially, a C₁₋₆alkoxy-carbonyl group), a carbamoyl group, which may have a substituent, corresponding to a carboxyl group protected by an amino group which may have a substituent, hydroxymethyl group, isocyanato group. Examples of a preferred X² include amino group, a C₂₋₆acylamino group corresponding to an amino group protected by a C₂₋₆acyl group, a C₁₋₆alkoxy-carbonylamino group corresponding to an amino group protected by a C₁₋₆alkoxy-carbonyl group, hydroxymethyl group, isocyanato group, depending on species of X¹.

[0087] Examples of a preferred X³ or X⁴ include hydrogen atom, an alkyl group, nitro group, amino group, a C₂₋₆acylamino group, a C₁₋₆alkoxy-carbonylamino group, carboxyl group, a C₁₋₁₀alkoxy-carbonyl group (particularly a C₁₋₆alkoxy-carbonyl group), a carbamoyl group which may have a substituent, hydroxymethyl group and isocyanato group.

[0088] A preferred X⁵ includes, for example, a carbamoyl group which may have a substituent, a C₁₋₆alkoxycarbonylamino group, a saturated aliphatic C₂₋₆acylamino group and an aromatic C₇₋₁₃acylamino group. A preferred X⁶ includes, for example, carboxyl group, a C₁₋₁₀alkoxy-carbonyl group, amino group, a C₂₋₆acylamino group, a C₁₋₆alkoxy-carbonylamino group and nitro group, depending on species of X⁵.

[0089] A preferred X⁷ or X⁸ includes, for example, a substituent exemplified as the preferred X³ or X⁴.

[0090] When such novel adamantane derivatives have an acidic group or a basic group, they may form salts.

[0091] Among the compounds shown by the formula (2), as a nitro group-containing adamantane derivative, there may be exemplified 1-amino-3-nitroadamantane, 1-amino-3-methyl-5-nitroadamantane, 1-amino-3,5-dimethyl-7-nitroadamantane, 1-amino-3,5-dinitroadamantane, 1-methoxycarbonylamino-3-nitroadamantane, 1,3-bis(methoxycarbonylamino)-5-nitroadamantane, 1-methoxycarbonylamino-3,5-dinitroadamantane, 1-ethoxycarbonylamino-3-nitroadamantane, 1-acetylamino-3-nitroadamantane, 1-acetylamino-3,5-dinitroadamantane, 1,3-bis(acetylamino)-5-nitroadamantane, 1-hydroxymethyl-3-nitroadamantane and 1-isocyanato-3-nitroadamantane.

[0092] As an adamantane derivative having an amino group or N-substituted amino group which may be protected by a protecting group, there may be mentioned, for example, 1-amino-3-isocyanatoadamantane, 1-amino-3-isocyanato-5-methyladamantane, 1-isocyanato-3-methoxycarbonylaminoadamantane, 1-isocyanato-3-(N-methylamino)adamantane and 1-acetylamino-3-isocyanatoadamantane.

[0093] Examples of an adamantane derivative having a carboxyl group which may be protected by a protecting group include 1-carboxy-3-hydroxymethyladamantane, 1,3-dicarboxy-5-hydroxymethyladamantane, 1-carboxy-3,5-bis(hydroxymethyl)adamantane, 1-carboxy-3-hydroxymethyl-5-methyladamantane, 1-hydroxymethyl-3-methoxycarbonylaminoadamantane, 1-ethoxycarbonyl-3-hydroxymethyladamantane, 1-hydroxymethyl-3-(N,N-dimethylcarbamoyl)adamantane, 1-isocyanato-3-methoxycarbonylaminoadamantane and 1-isocyanato-3-(N,N-dimethylcarbamoyl)adamantane.

[0094] An adamantane derivative having a hydroxymethyl group which may be protected by a protecting group includes, for example, 1-acetyloxymethyl-3-isocyanatoadamantane and 1-propionyloxymethyl-3-isocyanatoadamantane.

[0095] Among the adamantane derivatives shown by the formula (3), an adamantane derivative having a carbamoyl group which may have a substituent includes, for example, 1-carboxy-3-(N-methylcarbamoyl)adamantane, 1-carboxy-3-(N,N-dimethylcarbamoyl)adamantane, 1-carboxy-3-methyl-5-(N,N-dimethylcarbamoyl)adamantane, 1-methoxycarbonyl-3-(N,N-dimethylcarbamoyl)adamantane, 1-amino-3-(N,N-dimethylcarbamoyl)adamantane, 1-acetylamino-3-(N,N-dimethylcarbamoyl)adamantane, 1-methoxycarbonylamino-3-(N,N-dimethylcarbamoyl)adamantane and 1-(N,N-dimethylcarbamoyl)-3-nitroadamantane.

[0096] Examples of a nitro group-containing adamantane derivative include 1-methoxycarbonyl-3-nitroadamantane, 1,3-bis(methoxycarbonyl)-5-nitroadamantane, 1-methoxycarbonyl-3,5-dinitroadamantane, 1-methoxycarbonyl-3-methyl-5-nitroadamantane, 1-ethoxycarbonyl-3-nitroadamantane, 1-nitro-3-propoxycarbonylaminoadamantane and 1-nitro-3-phenoxy-carbonylaminoadamantane.

[0097] A substituted hydroxycarbonylamino group-containing adamantane derivative includes, for example, 1-methoxycarbonyl-3-methoxycarbonylaminoadamantane, 1-methoxycarbonyl-3-methoxycarbonylamino-5-methyladamantane, 1-ethoxycarbonyl-3-ethoxycarbonylaminoadamantane, 1-hydroxymethyl-3-methoxycarbonylaminoadamantane, 1-amino-3-methoxycarbonylaminoadamantane, 1-amino-3-methoxycarbonylamino-5-methyladamantane, 1-acetylamino-3-methoxycarbonylaminoadamantane and 1-acetylamino-3-ethoxycarbonylaminoadamantane.

[0098] A saturated aliphatic or aromatic amino group-containing adamantane derivative includes, for example, 1-acetylamino-3-carboxyadamantane, 1,3-bis(acetylamino)-5-carboxyadamantane, 1-acetylamino-3,5-dicarboxyadamantane, 1-acetylamino-3-carboxy-5-methyladamantane, 1-benzoylamino-3-carboxyadamantane, 1-acetylamino-3-hydroxymethyladamantane, 1-acetylamino-3-aminoadamantane, 1,3-bis(acetylamino)-5-aminoadamantane, 1-acetylamino-3,5-diaminoadamantane, 1-acetylamino-3-(N,N-dimethylamino)adamantane and 1-acetylamino-3-(N-methylamino)adamantane.

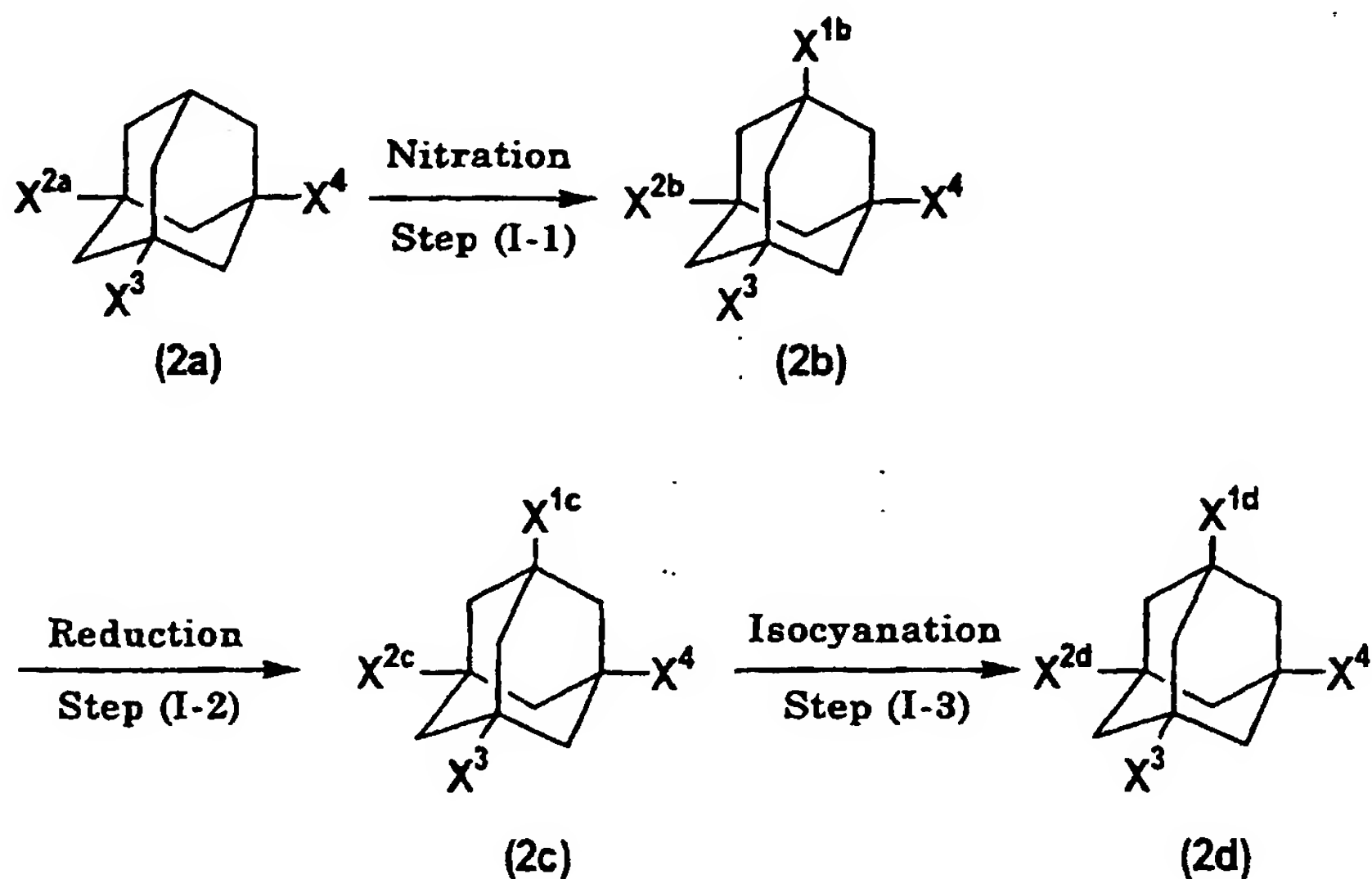
[0099] The adamantane derivative shown by the formula (2) or (3) may have other substituents, for example, a halo-

gen atom, an oxo group, a hydroxyalkyl group (e.g., hydroxy C₂₋₄alkyl groups such as 2-hydroxyethyl group), an acyl group (e.g., C₁₋₆acyl groups such as formyl, acetyl, propionyl, butyryl, isobutyryl, valeryl, isovaleryl and pivaloyl group), an alkoxycarbonyl group (e.g., C₁₋₆alkoxy-carbonyl group such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl, isobutoxycarbonyl, t-butoxycarbonyl and hexyloxycarbonyl group) and cyano group. [Production of adamantane derivatives]

[0100] The adamantane derivatives shown by the formulas (2) and (3) and an adamantane derivative having at least two substituents selected from the group consisting of a nitro group, an amino group or N-substituted amino group which may be protected by a protecting group, a carboxyl group which may be protected by a protecting group, a hydroxymethyl group which may be protected by a protecting group, and an isocyanato group, at a methine carbon atom of a bridgehead position of adamantane skeleton can be obtained by the following reaction step scheme (I) or (II), or by combining the reaction step scheme (I) and (II).

Reaction step scheme(I)

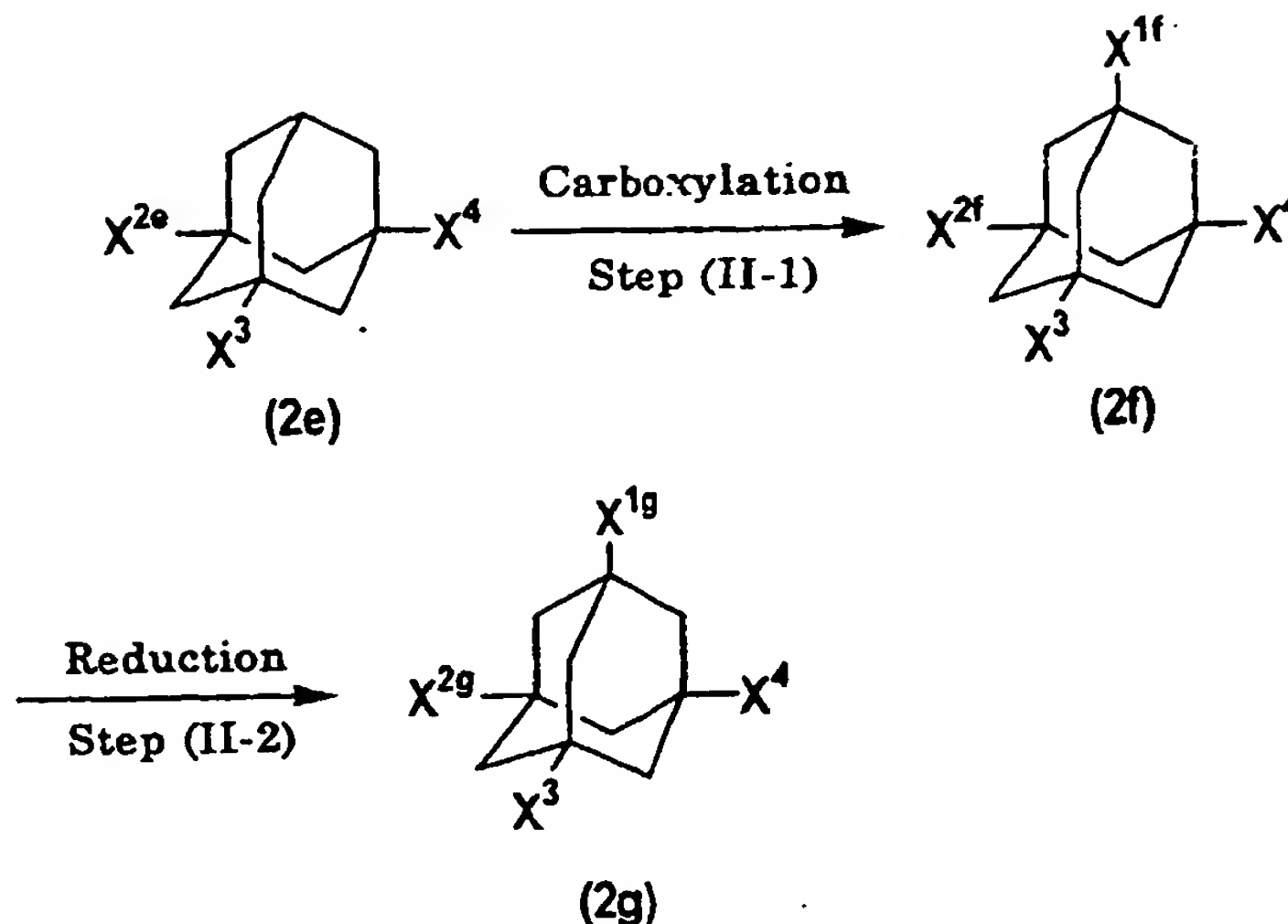
[0101]



wherein X^{1b} represents a nitro group; X^{1c} represents an amino group; X^{1d} represents an isocyanato group; X^{2a}, X^{2b}, X^{2c} and X^{2d} represent a hydrogen atom, a nitro group, an amino or N-substituted amino group which may be protected by a protecting group, a carboxyl group which may be protected by a protecting group, a hydroxymethyl group which may be protected by a protecting group, or an isocyanato group respectively; and X³ and X⁴ respectively have the same meanings as defined above).

Reaction step scheme (II)

[0102]



wherein X^{1f} represents a carboxyl group; X^{1g} represents a hydroxymethyl group; X^{2e} , X^{2f} and X^{2g} represents a hydrogen atom, a nitro group, an amino or N-substituted amino group which may be protected by a protecting group, a carboxyl group which may be protected by a protecting group, a hydroxymethyl group which may be protected by a protecting group, or an isocyanato group; and X^3 and X^4 each has the same meanings as defined above.)

[0103] The nitration (nitration reaction which derives compound (2b) from compound (2a)) of the step (I-1) in the reaction step scheme (I) may be carried out by the nitration method, i.e., the method of contacting a substrate with a nitrogen oxide at least, in the presence of the imide compound shown by the formula (1). A nitro group can be introduced to a methine carbon atom of a bridgehead position by the nitration. When X^{2a} in the compound (2a) is hydrogen atom, X^{2a} may be also converted into a nitro group according to reaction conditions. For example, nitration of an adamantane may give 1-nitroadamantane and/or 1,3-dinitroadamantane. Further, the nitration of 1-nitroadamantane, 1-carboxyadamantane and 1-hydroxyadamantane may give 1,3-dinitroadamantane, 1-carboxy-3-nitroadamantane and 1-hydroxy-3-nitroadamantane, respectively.

[0104] The reduction (reductive reaction which derives compound (2c) from compound (2b)) of the step (I-2) may be carried out by a conventional method such as catalytic hydrogenation process using hydrogen as a reducing agent and reduction process using a hydrogenation reducing agent.

[0105] In the catalytic hydrogenation, a simple substance of a metal such as platinum, palladium, nickel, cobalt, iron and copper, a compound containing such metal elements (e.g., platinum oxide, palladium black, palladium carbon and copper chromite) or the like may be used as a catalyst. The amount of the catalyst is practically about 0.02 to 1 mole relative to 1 mole of a substrate. Further, in a catalytic hydrogenation, the reaction temperature may be, for example, about -20 to 100 °C (e.g., about 0 to 90 °C). A hydrogen pressure is practically about 1 to 100 atm (e.g., about 1 to 50 atm).

[0106] In the reducing process using a hydrogenation reducing agent, the hydrogenation reducing agent to be used includes, for example, aluminium hydride, lithium aluminium hydride, lithium trialkoxyaluminium hydride, sodium boron hydride, diborane, bis-3-methyl-2-butylborane, a metal (e.g., zinc, tin, iron) acid, a sulfide and hydrazine. The reducing process using a hydrogenation reducing agent may be conducted also in the presence of a Lewis acid such as aluminium chloride anhydride and boron trifluoride. The amount of the hydrogenation reducing agent is usually about 1 mole or more (e.g., about 1 to 10 mole) relative to 1 mole of a substrate. In the reducing process using the hydrogenation reducing agent, a reaction temperature is practically about 0 to 200 °C (e.g., about 0 to 170 °C).

[0107] Incidentally, the reduction reaction (the catalytic hydrogenation and the process using the hydrogenation reducing agent) may be carried out in the presence of a solvent inert to the reduction reaction (e.g., an alcohol such as methanol and further a solvent exemplified in the nitration reaction such as a carboxylic acid, an ether, an ester and an

amide). Moreover, when reduction reaction is conducted by the catalytic hydrogenation, an acid such as hydrochloric acid may be added to the reaction system in order to improve the catalytic activity.

[0108] The nitro group X^{1b} of the compound (2b) is converted into an amino group by the reduction reaction. In the compound (2b), when X^{2b} is a nitro group, the nitro group may be also converted into an amino group according to reaction conditions. For example, the reduction of 1-nitroadamantane may give 1-aminoadamantane, and the reduction of 1,3-dinitroadamantane may give 1-amino-3-nitroadamantane and/or 1,3-diaminoadamantane. Further, the each reduction of 1-carboxy-3-nitroadamantane and 1-hydroxymethyl-3-nitroadamantane may give 1-amino-3-carboxyadamantane and 1-amino-3-hydroxymethyladamantane respectively.

[0109] The isocyanation (reaction deriving compound (2d) from compound (2c)) of the step (I-3) may be carried out by a conventional method, for example, the method using phosgene. The reaction of the compound (2c) with phosgene may be conducted, for example, in the presence or absence of a solvent at a temperature of about -10 to 100°C. The amount of phosgene is, for example, about 0.8 to 10 mole and preferably about 1 to 2 mole relative to 1 mole of the compound (2c).

[0110] The amino group X^{1c} of the compound (2c) may be converted into an isocyanato group by the reaction mentioned above. When X^{2c} of the compound (2c) is an amino group, the amino group may be converted into an isocyanato group according to conditions. For example, the isocyanation of 1-aminoadamantane may give 1-isocyanatoadamantane. Further, each of 1-amino-3-nitroadamantane, 1,3-diaminoadamantane, 1-amino-3-carboxyadamantane and 1-amino-3-hydroxymethyladamantane may be subjected to isocyanation to give 1-isocyanato-3-nitroadamantane, 1,3-diisocyanatoadamantane, 1-isocyanato-3-carboxyadamantane and 1-isocyanato-3-hydroxymethyladamantane respectively.

[0111] The carboxylation (reaction deriving compound (2f) from compound (2e)) of the step (II-1) in the reaction step scheme (II) may be carried out by the above-mentioned carboxylation, i.e., the process for contacting a substrate with at least carbon dioxide and oxygen in the presence of the imide compound shown by the formula (1). A carboxyl group can be introduced to a methine carbon atom at a bridgehead position of the compound (2e) by the carboxylation. When X^{2e} of the compound (2e) is a hydrogen atom, X^{2e} may be also converted to a carboxyl group according to reaction conditions. For example, an adamantane may be carboxylated to produce 1-carboxyadamantane and/or 1,3-dicarboxyadamantane as previously described. Further, the carboxylation of each 1-carboxyadamantane and 1-nitroadamantane may give 1,3-dicarboxyadamantane and 1-carboxy-3-nitroadamantane respectively.

[0112] The reduction (reaction introducing compound (2g) from compound (2f)) of the step (II-2) may be carried out by a conventional method such as catalytic hydrogenation using hydrogen as a reducing agent and a method using a hydrogenation reducing agent described for the step (I-2). In this step, a preferred hydrogenation reducing agent includes, for example, a sodium boron hydride-Lewis acid, aluminum hydride, lithium aluminum hydride, lithium trialkoxyaluminum hydride and diborane.

[0113] The reduction reaction may convert the carboxyl group X^{1f} of the compound (2f) may be converted to a hydroxymethyl group. Moreover, when X^{2f} of the compound (2f) is a carboxyl group, the carboxyl group may be also converted to a hydroxymethyl group according to reaction conditions. For example, the reduction of 1-carboxyadamantane gives 1-hydroxymethyladamantane, and the reduction of 1,3-dicarboxyadamantane gives 1-carboxy-3-hydroxymethyladamantane and/or 1,3-bis(hydroxymethyl)adamantane.

[0114] Incidentally, according to the species of substrates, a hydroxylmethyl group (a site corresponding to a hydroxyl group of the hydroxymethyl group), an amino group and a carboxyl group of the reaction component or the reaction product may be protected by the above protecting group before, after, or during the each step. The introduction and elimination of the protecting group for a hydroxymethyl group, an amino group and a carboxyl group may be carried out by a conventional method such as esterification, amidation, carbamation, carbonation, hydrolysis and hydrogenolysis, if necessary, using an acid, an alkali, an ion-exchange resin, a catalyst for hydrogenolysis or the like.

[0115] When an acyl group is used as a protecting group for a hydroxylmethyl group or an amino group (acyloxymethyl group or acylamino group is formed), the hydroxymethyl group or the amino group of the substrate may be protected by allowing to act an acylating agent on the substrate. Examples of the acylating agent include C_{2-6} aliphatic monocarboxylic acids such as acetic acid, propionic acid, n-butyric acid, isobutyric acid, valeric acid and pivalic acid (preferably C_{2-4} carboxylic acids), and reactive derivatives thereof [e.g., acid anhydrides such as acetic anhydride and valeric anhydride, acid halides such as acid chloride (e.g., acetyl chloride, propionyl chloride and butyryl chloride)]. When an acid anhydride or an acid halide is used as an acylating agent, the acylation reaction is usually carried out in the presence of a base in order to capture the acid which is a by-product in the reaction. As the base, there may be exemplified an inorganic base (e.g., a hydroxide of an alkali metal such as sodium hydroxide; a hydroxide of alkaline earth metal such as barium hydroxide; carbonate of an alkaline metal such as sodium carbonate; a carbonate of an alkaline earth metal such as barium carbonate; a hydrogencarbonate of an alkaline metal such as sodium hydrogencarbonate); and an organic base (e.g., a tertiary amine such as triethylamine and N-methylpiperidine; a basic heterocyclic compound containing a nitrogen atom such as pyridine; an alkoxide of an alkali metal such as sodium methoxide and sodium ethoxide). The acylating agent may be used singly or in combination of two or more.

[0116] For example, 1-acetylamino-3-nitroadamantane can be obtained by acting acethyl chloride on 1-amino-3-nitroadamantane in the presence of the base.

[0117] When a substituted hydroxycarbonyl group is used as a protecting group for a hydroxymethyl group or an amino group, the hydroxyl group or the amino group may be protected by reacting a substrate with a halocarbonate to obtain a compound having a carbonate group or carbamate group. The reaction may be usually carried out in the presence of a base. As the base, the similar base to one exemplified above may be used.

[0118] When a carbamoyl group is used as a protecting group for a hydroxymethyl group, the hydroxymethyl group may be protected, for example, by reacting a substrate with an isocyanate compound, if necessary, in the presence of the base exemplified above to obtain a compound having a carbamoyloxy group.

[0119] Moreover, an adamantane derivative having N-substituted amino group may be produced, for example, by reacting a substrate with a hydrocarbon halide (e.g., aliphatic hydrocarbon halide such as iodomethane, iodoethane, iodobutane, bromomethane, bromoethane, bromobutane, chloromethane and chloroethane). The reaction may be conducted in the presence of a de-hydrogen halide agent (an agent for eliminating a hydrogen halide). As the de-hydrogen halide agent, a base, for example, the above exemplified may be practically used. The reaction may be conducted in solvent inert to the reaction. As such solvent, use may be made of exemplified solvents for the nitration reaction such as a hydrocarbon halide, an ether, an ester and an amide.

[0120] When a substituted hydroxyl group (e.g., an alkoxy group) protects a carboxyl group [(i.e., when a substituted hydroxycarbonyl group (an ester group)) is formed], the carboxyl group may be protected by reacting a carboxyl group-containing compound or derivative thereof (e.g., an acid halide such as an acid chloride) with an alcohol (e.g., methanol, ethanol) or reactive derivative thereof (e.g., lower alkyl ester), if necessary, in the presence of an acid (e.g., a mineral acid such as hydrochloric acid and sulfuric acid) or an base (e.g., the base exemplified above) to produce a compound having the corresponding ester group. The lower alkyl ester includes, for example, acetic acid-C₁₋₄alkyl ester such as methyl acetate and ethyl acetate or the corresponding propionate (e.g., methyl propionate, ethyl propionate). For example, 1-methoxycarbonyl-3-nitroadamantane may be obtained by reacting 1-carboxy-3-nitroadamantane with methanol in the presence of an acid, or by acting thionyl chloride on 1-carboxy-3-nitroadamantane followed by reacting with methanol in the presence of a base.

[0121] Moreover, when a carboxyl group is converted into a group having an amide bond with use of an amino group as a protecting group for the carboxyl group (i.e., when an N-substituted or unsubstituted carbamoyl group is formed), a condition of a conventional process for forming an amido bond may be applied. The process for forming an amido bond may be carried out, for example, by following methods:

(a) a method by a mixed acid anhydride, i.e., a method which comprises reacting a compound having a carboxyl group with an acid halide (e.g., acetyl chloride, propionyl chloride, acetyl bromide) to produce a mixed acid anhydride followed by reacting the given mixed acid anhydride with an amine compound;

(b) a method by an active ester, i.e., a method which comprises converting a substrate into an active ester thereof, such as p-nitrophenylester, an ester with N-hydroxysuccinimide, an ester with 1-hydroxybenzotriazol or the like followed by reacting the given ester with an amine compound;

(c) a method by a carbodiimide, i.e., a method which condenses an amine compound with a substrate in the presence of an activating agent such as dicyclohexylcarbodiimide and carbonyldiimidazol; or

(d) a method which comprises converting a substrate into a carboxylic anhydride thereof by a dehydrator such as acetic anhydride followed by reacting the given carboxylic anhydride with an amine compound, or a method which comprises converting a substrate to an acid halide thereof followed by reacting the acid halide with an amine compound.

[0122] The amine compound used in the amide bond forming reaction includes, for example, ammonia or a derivative thereof (e.g., ammonium halide such as ammonium chloride), a primary amine, a secondary amine, hydrazine or a derivative thereof (e.g., alkoxycarbonylhydrazine such as t-butoxycarbonylhydrazine, alkoxycarbonylhydrazine such as benzyloxycarbonylhydrazine).

[0123] For example, the reaction of an acid halide with an amine compound may be carried out in a suitable solvent, in the presence of an basic compound. As the basic compound, use may be made of a basic compound exemplified for the reaction of the compound (1a) having an amino group or the compound (1d) with a hydrocarbon halide and the like.

[0124] Moreover, as the solvent, an organic solvent (e.g., an ether, an ester, an amide) exemplified for the nitration reaction may be employed.

[0125] Furthermore, the compound having a carbamoyl group may be obtained by reacting a compound having an ester group (e.g., an alkoxycarbonyl group, an aryloxycarbonyl group, an aralkyloxycarbonyl group) as a protected carboxyl group with the amine compound in the presence of a catalyst comprising a metal compound.

[0126] Examples of the metal compound used in the reaction (the amidation reaction) include a conventional catalyst for transesterification (including a catalyst for transferring an ester to an amide), for example, a transition metal com-

pound such as a compound comprising Group 3B element of the Periodic Table of Elements (e.g., aluminum compound such as AlCl_3), a compound comprising Group 4A element of the Periodic Table of Elements (e.g., titanium compound such as TiCl_4), a compound comprising Group 3A element (e.g., samarium compound such as SmI_2) of the Periodic Table of Elements.

5 [0127] The amount of the catalyst may be liberally selected within a broad range, for example, about 0.1 mole% to 1 equivalent, preferably about 0.5 to 50 mole%, and more preferably about 1 to 25 mole% (e.g., about 5 to 20 mole%) relative to a compound having an ester group.

[0128] The ratio of the amine compound to the ester group-containing compound is, for example, about 0.5 to 5 mole, preferably about 0.8 mole or more (e.g., about 0.8 to 5 mole), and specifically about 1 mole or more (e.g., about 1 to 3 mole, in particular about 1 to 1.5 mole) of ammonia or the like relative to 1 equivalent of the ester group-containing compound.

10 [0129] The amidation reaction may be carried out in the presence or absence of a solvent inert to the reaction. As the reaction solvent, there may be exemplified an aliphatic hydrocarbon, an alicyclic hydrocarbon, an aromatic hydrocarbon, a ketone, an ether, a non-protonic polar solvent and a mixture thereof. The reaction temperature may be selected within the range of, for example, about 0 to 150 °C, and preferably about 25 to 120 °C.

15 [0130] The adamantane derivative shown by the formula (2) and (3) of the present invention can be concretely produced as follows.

[0131] For example, among compounds shown by the formula (2), a compound having a nitro group and an amino group which may have a protecting group or a substituent can be produced through the steps (I-1) and (I-2). A compound having a nitro group and an isocyanato group can be produced through the steps (I-1), (I-2) and (I-3). A compound having a nitro group and a hydroxymethyl group which may be protected by a protecting group may be obtained through the steps (I-1), (II-1) and (II-2).

[0132] A compound having an amino group which may have a protective group or a substituent, and an isocyanato group may be produced through the steps (I-1), (I-2) and (I-3).

25 [0133] A compound having a carboxyl group, which may be protected by protective group, and a hydroxymethyl group which may be protected by a protecting group may be obtained, for example, through the step (II-1) and (II-2). A compound having a carboxyl group which may be protected by a protecting group, and an isocyanato group may be obtained through the steps (I-1), (I-2), (I-3) and (II-1).

[0134] A compound having a hydroxymethyl group which may be protected by a protecting group, and an isocyanato group may be produced through the steps (I-1), (I-2), (I-3), (II-1) and (II-2).

30 [0135] Among the compounds shown by the formula (3), a compound having a carbamoyl group which may have a substituent, and a carboxyl group may be obtained through the step (II-1) and the step of introducing an amino group to a carboxyl group (the amide group-forming step). A compound having a carbamoyl group which may have a substituent, and a substituted hydroxycarbonyl group may be obtained through the step (II-1), the step for introducing an amino group to a carboxyl group and the step for introducing a substituted hydroxyl group to another carboxyl group (the ester group-forming step). A compound having a carbamoyl group which may have a substituent, and an amino group which may have a protecting group or a substituent may be obtained through the steps (I-1), (I-2), (II-1) and the step of introducing an amino group to the carboxyl group. A compound having a carbamoyl group which may have a substituent, and a nitro group may be obtained through the steps (I-1), (II-1) and the step of introducing an amino group to the carboxyl group.

40 [0136] A compound having a nitro group and a substituted hydroxycarbonyl group may be produced through the steps (I-1), (II-1), and the step of introducing a substituted hydroxyl group to the carboxyl group. A compound having a substituted hydroxycarbonylamino group and a substituted hydroxycarbonyl group may be obtained through the steps (I-1), (I-2), (II-1) and the step of introducing the substituted hydroxycarbonyl group to an amino group (the carbamate group-forming step) and the step of introducing a substituted hydroxyl group to the carboxyl group. A compound having a substituted hydroxycarbonylamino group and, a hydroxyl group may be protected by a protecting group through the steps (I-1), (I-2), (II-1), (II-2), and the step of introducing an amino group to the substituted hydroxycarbonyl group. A compound having a substituted hydroxycarbonylamino group and an amino group which may be protected by a protecting group may be obtained through the steps (I-1), (I-2), (I-3), and the step of introducing an substituted hydroxycarbonyl group to the amino group. A compound having a saturated aliphatic or aromatic acylamino group and a carboxyl group may be obtained through the steps (I-1), (I-2), (II-1), and the step of introducing an acyl group to an amino group. A compound having a saturated aliphatic or aromatic acylamino group and a hydroxymethyl group which may be protected by a protecting group may be obtained through the steps (I-1), (I-2), (II-1), (II-2), and the step of introducing an acyl group to an amino group. A compound having a saturated aliphatic or aromatic acylamino group and an amino group which may be protected by an alkyl group may be obtained through the steps (I-1), (I-2), and the step of introducing an acyl group to an amino group. The introduction of an amino group or a substituted hydroxyl group to a carboxyl group, introduction of a substituted hydroxycarbonyl group to an amino group, and introduction of an acyl group to an amino group may be carried out by the above method for introducing a protecting group.

[0137] Further, the diaminoadamantane derivative (compound (2j)) having at least two groups of amino groups or N-substituted amino groups, which may be protected by a protecting group, at bridgehead position of adamantane skeleton may be obtained by nitrating the compound (compound (2h)) in which X^{2a} of the compound (2a) is a hydrogen atom or a nitro group according to the step (I-1) to form a dinitro body (compound (2i)) in which X^{1b} and X^{2b} of the compound (2b) are nitro groups, and then reducing it according to the step (I-2) to convert into a diamino body in which X^{1c} and X^{2c} of the compound (2c) are amino groups and, if necessary, introducing a protecting group or a substituent to the amino group. In the method, since the diamino body is directly formed in the form of not salt but free, the alternation or denaturation, decomposition or decrease of recover efficiency, each occurring when salt of a diamino body becomes free may be avoided. Therefore, the diamino adamantane derivative may be efficiently produced with high yield.

INDUSTRIAL APPLICABILITY

[0138] In the method of the present invention, a substrate may be directly nitrated and/or carboxylated efficiently even in a mild or moderate condition since an imide compound shown by the formula (1) is combined with at least one reacting agent selected from (i) a nitrogen oxide and (ii) a mixture of carbon monoxide and oxygen. Moreover, to a substrate, at least one functional group selected from a nitro group and a carboxyl group can be introduced to produce a nitro compound and/or carboxy compound with high conversion and selectivity even in the mild or moderate condition.

[0139] Moreover, nitrogen oxide, which causes environmental pollution, is efficiently utilized to form a nitro compound may be produced with high conversion and selectivity. Further, a carboxy compound having more carbon atoms than that of a substrate may be efficiently produced by a simple operation through fewer steps.

[0140] Further, in the present invention, a novel adamantane derivative useful for a high functional material may be provided. A diamino body of adamantane can be produced in high yield.

EXAMPLES

[0141] The following examples are intended to describe this invention in further detail and should by no means be interpreted as defining the scope of the invention. Incidentally, infrared absorption spectra were measured after purifying the reaction product by column chromatography.

Example 1

[0142] Into a flask, 1 mmole of adamantane, 0.05 mmole of N-hydroxyphthalimide and 5 ml of acetic acid were added to mix and then the flask was equipped with a gas bag (about 1L) of nitrogen monoxide NO. The mixture was reacted for 8 hours at 100°C with stirring. The reaction products were analyzed by gas chromatography, and, as a result, The conversion of adamantane was 95%, and nitroadamantane (yield 30%), adamantanol (yield 17%) and acetyloxyadamantane (yield 33%) were formed.

Example 2 to 5

[0143] Into a flask, 1 mmole of adamantane, 0.05 mmole of N-hydroxyphthalimide and 5 ml of the solvent represented in Table 1 were added to mix, and then the flask was equipped with a gas bag (about 1L) of nitrogen monoxide NO. The mixture was heated to 100°C with stirring. After the period of time shown in Table 1, the reaction products were analyzed by gas chromatography, and, as a result, nitro compounds were formed with conversions and yields represented in Table 1.

[0144] Meanings of the symbols in Table 1 are as follows.

BzCN: benzonitrile

AcOH: acetic acid

DCE: dichloroethane

Com. 1: adamantanol

Com. 2: acetyloxyadamantane

Com. 3: nitroadmantane

Com. 4: adamantanediol

Com. 5: nitroadamantano

Table 1

	Solvents	Times (hr)	Conversions(%)	Yields(%)				
				Com.1	Com.2	Com.3	Com.4	Com.5
Ex.2	BzCN	5	76	16	0	19	9	8
Ex.3	AcOH	10	95	11	22	20	10	10
Ex.4	AcOH	16	99	4	17	30	15	18
Ex.5	DCE	16	64	19	0	18	6	4

Example 6 to 8

[0145] Into a flask, 1 mmole of adamantane, 0.05 mmole of N-hydroxyphthalimide and 5 ml of the solvent shown in Table 2 were added to mix and the flask was purged by nitrogen monoxide NO (about 1L) and oxygen O₂ (about 1L). The mixture was reacted for 10 hours at the temperatures shown in Table 2, with stirring. Reaction products were analyzed by gas chromatography, and, as a result, nitro compounds were formed with yields represented in Table 2.

[0146] Meanings of the symbols shown in Table 2 are as follows.

AcOH: acetic acid
 AcCN: acetonitrile
 BzCN: benzonitrile
 DCE: dichloroethane
 Com. 1: adamantanol
 Com. 2: acetyloxyadamantane
 Com. 3: nitroadmantane
 Com. 4: adamantanediol
 Com. 5: nitroadamantanol

Table 2

	Solvents	Temperatures (°C)	Conversions(%)	Yields(%)				
				Com.1	Com.2	Com.3	Com.4	Com.5
Ex.6	AcOH	100	99	4	11	43	10	21
Ex.7	AcCN+DCE	60	89	5	10	50	6	11
Ex.8	BzCN+AcOH	100	99	1	1	79	1	3

Example 9

[0147] An eggplant type flask with side arm was dipped in iced water and reduced pressure. Into the flask, not only nitrogen monoxide and oxygen was introduced from a gas bag (1L). The flask was filled with reddish-brown gas, and then the reddish-brown gas sedimented to form blue liquid which comprised N₂O₃ as a main component was formed with sedimentation of. The introductions of the nitrogen monoxide and oxygen were repeated to produce about 1.5 ml of the blue liquid. The blue liquid was frozen with use of liquid nitrogen.

[0148] 1.8g (0.024 mole based on N₂O₃ basis) of the frozen blue liquid, 1 mmole of adamantane, 0.05 mmole of N-hydroxyphthalimide and 5ml of acetic acid were mixed, and then the mixture was reacted for 10 hours at 100°C with stirring. The reaction products were analyzed by gas chromatography, and, as a result, nitroadamantane (yield 81%) was formed with conversion of 99%.

Example 10

[0149] The nitration reaction was effected in the same manner as Example 9 except that 1.8g (0.024 mole based on N₂O₃) of the frozen blue liquid, 1 mole of adamantane, 0.05mmole of N-hydroxyphthalimide and 5ml acetic acid were

mixed and then the mixture was reacted for 16 hours at 25°C with stirring. As a result, nitroadamantane was formed. The conversion of adamantane was 83% and the yield of the nitroadamantane was 72%.

Example 11

[0150] Into a flask, 1 mmole of adamantane, 0.1 mmole of N-hydroxyphthalimide, 2 ml of nitrogen dioxide (N₂O), 6 ml of benzonitrile (6ml) and 1.2 ml of acetic acid were added and stirred for 12 hours at 60°C in an atmosphere of nitrogen monoxide (NO). The reaction products were analyzed by gas chromatography, and, as a result, the conversion of adamantane was 98%, nitroadamantane (yield 68%), adamantanol (yield 6%) and acetyloxyadamantane (yield 4%) were formed.

Example 12

[0151] The reaction was effected in the same manner as Example 11 except for stirring in an atmosphere of oxygen instead of the atmosphere of nitrogen oxide (NO)). Nitroadamantane (yield 78%), adamantanol (yield 1%), acetyloxyadamantane (yield 1%) and adamantanone (yield 3%) were formed. The conversion of adamantane was 98%.

Example 13

[0152] The reaction was effected in the same manner as Example 11 except for stirring in an atmosphere of an inert gas (argon) instead of the atmosphere of nitrogen oxide (NO)). Nitroadamantane (yield 76%), adamantanol (yield 1%), acetyloxyadamantane (yield 6%) and adamantanone (yield 6%) were formed. The conversion of adamantane was 97%.

Example 14

[0153] Into a flask, 1 mmole of ethylbenzene, 0.05 mmole of N-hydroxyphthalimide and 5 ml of acetic acid were added to mix and the flask was equipped with a gas bag (about 1L) of nitrogen monoxide NO. The mixture was reacted for 8 hours at 100°C with stirring. The reaction products were analyzed by gas chromatography, and, as a result, the conversion of ethylbenzene was 85%, and 1-nitroethylbenzene (yield 14%), 1-hydroxyethylbenzene (yield 18%) and 1-acetyloxyethylbenzene (yield 30%) were formed.

Example 15

[0154] Into a flask, 1 mmole of adamantane, 0.1 mmole of N-hydroxyphthalimide and 6 ml of acetic acid were added to mix. The flask was purged by nitrogen monoxide NO (about 1L) and oxygen O₂ (about 1L), and then the mixture was reacted for 20 hours at 110°C with stirring. The reaction products were analyzed by gas chromatography, and, as a result, the conversion of adamantane was 90%, and 1-nitroadamantane (yield 64%) and 1,3-dinitroadamantane (yield 12%) were formed.

Example 16

[0155] The operation was effected in the same manner as Example 15 except for using 1-nitroadamantane instead of adamantane. 1,3-dinitroadamantane (yield 80%) was formed. The conversion of 1-nitroadamantane was 90%. Incidentally, when the reaction time was 6 hours, the conversion of 1-nitroadamantane was 33% and the yield of 1,3-dinitroadamantane was 27%.

Pale yellow solid

Mass spectral data [M]⁺: 226

IR(cm⁻¹) : 1560, 1360, 750

Example 17

[0156] Into a flask, 1 mmole of adamantane, 0.1 mmole of N-hydroxyphthalimide, 6 ml of benzonitrile and 1 ml of acetic acid were added to mix and the flask was equipped with a gas bag (about 1L) of nitrogen monoxide NO. The mixture was reacted for 20 hours at 100°C with stirring. The reaction products were analyzed by gas chromatography, and, as a result, the conversion of adamantane was 92%, and 1-benzoylaminoadamantane (yield 65%), 1-adamantanol (yield 7%), 1-nitroadamantane (yield 6%), 1-acetyloxyadamantane (yield 2%) and 2-adamantanone (yield 2%) were formed.

Example 18

5 [0157] Into a flask, 2 mmole of toluene, 0.2 mmole of N-hydroxyphthalimide, 6 ml of 1,2-dichloroethane and 1.2 ml of acetonitrile were added to mix. The mixture was reacted for 12 hours at 60°C with stirring in an atmosphere of nitrogen dioxide NO₂. The reaction products were analyzed by gas chromatography, and, as a result, the conversion of toluene was 47%, and 2-nitrotoluene (yield 18%), nitromethylbenzene (yield 9%) and 4-nitrotoluene (yield 9%) were formed.

Example 19

10 [0158] The operation was effected in the same manner as Example 18 except for conducting the reaction after purged by nitrogen monoxide NO and oxygen O₂ (molar ratio 1:1) to reaction system instead of nitrogen dioxide NO₂. 2-nitrotoluene (yield 20%), nitromethylbenzene (yield 7%) and 4-nitrotoluene (yield 3%) were formed. The conversion of toluene was 52%.

15 Example 20

[0159] The operation was effected in the same manner as Example 19 except for using ethylbenzene instead of toluene. The conversion of ethylbenzene was 100%, and 1-nitroethylbenzene (yield 13%), 2-nitro-1-ethylbenzene (yield 21%) and 4-nitro-1-ethylbenzene (yield 18%) were formed.

20

Example 21

25 [0160] The operation was effected in the same manner as Example 20 except for using nitrogen dioxide NO₂ and oxygen O₂ (molar ratio 1:1) instead of nitrogen monoxide NO and oxygen O₂ and reacting for 8 hours. The conversion of ethylbenzene was 100%, and 1-nitroethylbenzene (yield 15%), o-nitroethylbenzene (yield 19%) and m-nitroethylbenzene (yield 13%) were formed.

Example 22

30 [0161] The operation was effected in the same manner as Example 20 except for using nitrogen dioxide NO₂ and nitrogen monoxide NO (molar ratio 1:1) instead of nitrogen monoxide NO and oxygen O₂ and reacting for 8 hours. The conversion of ethylbenzene was 91%, and 1-nitroethylbenzene (yield 11%), o-nitroethylbenzene (yield 3%) and acetophenone (yield 14%) were formed.

35 Example 23

40 [0162] Into a flask, 1 mmole of adamantane, 0.05 mmole of N-hydroxyphthalimide, 15 mmole of nitrogen dioxide (NO₂) and 3 ml of acetonitrile were added and stirred for 5 hours at 60°C in an atmosphere of oxygen. The reaction products were analyzed by gas chromatography, and, as a result, the conversion of adamantane was 97%, and nitroadamantane (yield 65%), dinitroadamantane (yield 1%), adamantanol (yield 1%), acetyloxyadamantane (yield 3%) and adamantanone (yield 2%) were formed.

Example 24

45 [0163] The reaction was effected in the same manner as Example 23 except that the amount of N-hydroxyphthalimide was 0.1 mmole and the reaction time was 3 hours. The conversion of adamantane was 98%, and nitroadamantane (yield 69%), adamantanol (yield 1%), acetyloxyadamantane (yield 2%) and adamantanone (yield 2%) were formed.

Example 25

50

[0164] Into a flask, 1 mmole of adamantane, 0.05 mmole of N-hydroxyphthalimide, 15 mmole of nitrogen dioxide (NO₂) and 3 ml of trifluoromethylbenzene were added and stirred for 5 hours at 60°C in an atmosphere of oxygen. The reaction products were analyzed by gas chromatography, and, as a result, the conversion of adamantane was 79%, and nitroadamantane (yield 57%), adamantanol (yield 6%) and adamantanone (yield 4%) were formed.

55

Example 26

[0165] The reaction was effected in the same manner as Example 25 except that the amount of N-hydroxyphthalimide

was 0.1 mmole. The conversion of adamantane was 96%, and nitroadamantane (yield 66%), adamantanol (yield 4%) and adamantanone (yield 5%) were formed.

Example 27

5 [0166] Into a flask, 1 mmole of adamantane, 0.05 mmole of N-hydroxyphthalimide, 15 mmole of nitrogen dioxide (NO_2), 1 ml of acetonitrile and 2 ml of trifluoromethylbenzene were added and stirred for 5 hours at 60°C in an atmosphere of oxygen. The reaction products were analyzed by gas chromatography, and, as a result, the conversion of adamantane was 90%, and nitroadamantane (yield 73%), adamantanol (yield 2%), acetyloxyadamantane (yield 1%) and
10 adamantanone (yield 3%) were formed.

Example 28

15 [0167] The reaction was effected in the same manner as Example 27 except that the amount of N-hydroxyphthalimide was 0.1 mmole. The conversion of adamantane was 95%, and nitroadamantane (yield 76%), adamantanol (yield 1%), acetyloxyadamantane (yield 1%) and adamantanone (yield 3%) were formed.

Example 29

20 [0168] The reaction was effected in the same manner as Example 28 except that the amount of acetonitrile was 0.5 ml and that the amount of trifluoromethylbenzene was 2.5 ml. The conversion of adamantane was 89%, and nitroadamantane (yield 70%), adamantanol (yield 1%), acetyloxyadamantane (yield 1%) and adamantanone (yield 4%) were formed.

Example 30

25 [0169] Into a flask, 1 mmole of adamantane, 0.05 mmole of N-hydroxyphthalimide, 15 mmole of nitrogen dioxide (NO_2) and 3 ml of dichloroethane were added and stirred for 5 hours at 60°C in an atmosphere of oxygen. The reaction products were analyzed by gas chromatography, and, as a result, the conversion of adamantane was 97%, and nitroadamantane (yield 57%), adamantanol (yield 12%) and adamantanone (yield 4%) were formed.
30

Example 31

35 [0170] Into a flask, 1 mmole of adamantane, 0.1 mmole of N-hydroxyphthalimide, 15 mmole of nitrogen dioxide (NO_2) and 3 ml of acetic acid were added and stirred for 5 hours at 60°C in an atmosphere of oxygen. The reaction products were analyzed by gas chromatography, and, as a result, the conversion of adamantane was 96%, and nitroadamantane (yield 75%), adamantanol (yield 1%), acetyloxyadamantane (yield 5%) and adamantanone (yield 4%) were formed.

Example 32

40 [0171] Into a flask, 1 mmole of adamantane, 0.1 mmole of N-hydroxyphthalimide, 0.0005 mmole of acetylacetonatomanganese(II) $\text{Mn}(\text{AA})_2$ and 5 ml of acetic acid were added to mix and the flask was equipped with a gas bag (about 1L) of nitrogen monoxide NO . The mixture was reacted for 8 hours at 100°C with stirring. The reaction products were analyzed by gas chromatography, and, as a result, the conversion of adamantane was 95%, and nitroadamantane
45 (yield 75%) was formed.

Example 33

50 [0172] The reaction was effected in the same manner as Example 32 except for using acetylacetonatomanganese(III) $\text{Mn}(\text{AA})_3$ instead of $\text{Mn}(\text{AA})_2$. The conversion of adamantane was 72%, and nitroadamantane (yield 66%) was formed.

Example 34

55 [0173] The reaction was effected in the same manner as Example 32 except for using molybdic acid H_2MoO_4 instead of $\text{Mn}(\text{AA})_2$. The conversion of adamantane was 62%, and nitroadamantane (yield 57%) was formed.

Example 35

[0174] The reaction was effected in the same manner as Example 32 except for using acetylacetonatoiron(III) $\text{Fe}(\text{AA})_3$ instead of $\text{Mn}(\text{AA})_2$. The conversion of adamantane was 56%, and nitroadamantane (yield 50%) was formed.

Example 36

[0175] The reaction was effected in the same manner as Example 32 except for using manganese acetate $\text{Mn}(\text{Oac})_2$ instead of $\text{Mn}(\text{AA})_2$. The conversion of adamantane was 77%, and nitroadamantane (yield 72%) was formed.

Example 37

[0176] The reaction was effected in the same manner as Example 32 except for using 0.0001 mmole of acetylacetonatocobalt(II) $\text{Co}(\text{AA})_2$ instead of $\text{Mn}(\text{AA})_2$. The conversion of adamantane was 82%, and nitroadamantane (yield 75%) was formed.

Example 38

[0177] The reaction was effected in the same manner as Example 32 except for using acetylacetonatonickel(II) $\text{Ni}(\text{AA})_2$ instead of $\text{Mn}(\text{AA})_2$. The conversion of adamantane was 54%, and nitroadamantane (yield 49%) was formed.

Example 39

[0178] The reaction was effected in the same manner as Example 32 except for using acetylacetonatochromium(III) $\text{Cr}(\text{AA})_3$ instead of $\text{Mn}(\text{AA})_2$. The conversion of adamantane was 72%, and nitroadamantane (yield 66%) was formed.

Example 40

[0179] The reaction was effected in the same manner as Example 32 except for using acetylacetonatocopper(II) $\text{Cu}(\text{AA})_2$ instead of $\text{Mn}(\text{AA})_2$. The conversion of adamantane was 52%, and nitroadamantane (yield 46%) were formed.

Example 41

[0180] The reaction was effected in the same manner as Example 32 except for using acetylacetonatocopper(III) $\text{Cu}(\text{AA})_3$ instead of $\text{Mn}(\text{AA})_2$. The conversion of adamantane was 48%, and nitroadamantane (yield 42%) were formed.

Example 42

[0181] Into a flask, 1 mmole of 1-carboxyadamantane, 0.1 mmole of N-hydroxyphthalimide and 6 ml of acetic acid were added to mix. The mixture was purged by nitrogen monoxide NO (about 1L) and oxygen O_2 (about 1L), and then reacted for 20 hours at 110°C with stirring. The reaction products were analyzed by gas chromatography, and, as a result, the conversion of 1-carboxyadamantane was 90%, and 1-carboxy-3-nitroadamantane (yield 80%) was formed.

Pale yellow solid

Mass spectral data $[\text{M}]^+$: 225

IR(cm^{-1}) : 2990, 1620, 1560

Example 43

[0182] The reaction was effected in the same manner as Example 42 except for using 1-hydroxymethyladamantane instead of 1-carboxyadamantane. The conversion of 1-hydroxymethyladamantane was 90%, and 1-hydroxymethyl-3-nitroadamantane (yield 70%) was formed.

Pale yellow solid

Mass spectral data $[\text{M}]^+$: 211

IR(cm^{-1}) : 3350, 1550, 1370

Example 44

5 [0183] To acetic acid, the mixture of 10 mmole of adamantane, 1 mmole of N-hydroxyphthalimide (NHPI) and 0.005 mmole of acetylacetonatocobalt(II) $\text{Co}(\text{AA})_2$ was charged and the container was equipped with a gas bag charged with mixed gas (mixed gas comprised 2L of carbon monoxide and 0.5L of oxygen; pressure: $5\text{kg}/\text{cm}^2$). The mixture was stirred for 6 hours at 60°C . The products in the reaction mixture were analyzed by gas chromatography, and, as a result, the conversion of adamantane was 76%, and 1-carboxyadamantane (yield 70%) was formed.

Example 45

10 [0184] The reaction was effected in the same manner as Example 44 except for using acetylacetonatomanganese(II) $\text{Mn}(\text{AA})_2$ instead of $\text{Co}(\text{AA})_2$. The conversion of adamantane was 68%, and 1-carboxyadamantane (yield 62%) were formed.

15 Example 46

[0185] The reaction was effected in the same manner as Example 44 except for using acetonitrile instead of acetic acid. The conversion of adamantane was 73%, and 1-carboxyadamantane (yield 69%) were formed.

20 Example 47

[0186] The reaction was effected in the same manner as Example 44 except for using dichloroethane instead of acetic acid. The conversion of adamantane was 81%, and 1-carboxyadamantane (yield 75%) were formed.

25 Example 48

[0187] The reaction was effected in the same manner as Example 44 except that the reaction temperature was 80°C . The conversion of adamantane was 87%, and 1-carboxyadamantane (yield 81%) was formed.

30 Example 49

[0188] The reaction was effected in the same manner as Example 44 except for using 1-methyladamantane instead of adamantane. The conversion of 1-methyladamantane was 71%, and 1-carboxy-3-methyladamantane (yield 66%) was formed.

35 Example 50

[0189] The reaction was effected in the same manner as Example 44 except for using toluene instead of adamantane. The conversion of toluene was 67%, and phenyl acetate (yield 61%) were formed.

40 Example 51

[0190] The reaction was effected in the same manner as Example 44 except for using ethylbenzene instead of adamantane and that the pressure of the mixed gas was $10\text{kg}/\text{cm}^2$. The conversion of ethylbenzene was 71%, and 1-phenylpropionic acid (yield 56%) was formed.

Example 52

50 [0191] The reaction was effected in the same manner as Example 44 except for using fluorene instead of adamantane and that the pressure of the mixed gas was $10\text{kg}/\text{cm}^2$. The conversion of fluorene was 73%, and 9-carboxyfluorene (yield 69%) were formed.

Example 53

55 [0192] To the solvent mixture of 3ml of acetic acid and 3ml of 1,2-dichloroethane, a mixture of 10 mmole of tetrahydrodicyclopentadiene, 3 mmole of N-hydroxyphthalimide(NHPI) and 0.05 mmole of acetylacetonatocobalt(II) $\text{Co}(\text{AA})_2$ was charged. The reaction mixture was stirred for 15 hours at 85°C in an atmosphere of mixed gas of carbon monoxide and air (partial pressure of carbon monoxide: $45\text{kg}/\text{cm}^2$, partial pressure of air: $1\text{kg}/\text{cm}^2$). The products in the reaction

mixture were analyzed by gas chromatography, and, as a result, the conversion of tetrahydrodicyclopentadiene was 68%, and 1-carboxytetrahydrodicyclopentadiene (yield 38%) was formed.

Example 54

[0193] The reaction was effected in the same manner as Example 53 except for using acetylacetonatomanganese(II) $\text{Mn}(\text{AA})_2$ instead of $\text{Co}(\text{AA})_2$. The conversion of tetrahydrodicyclopentadiene was 66%, and 1-carboxytetrahydrodicyclopentadiene (yield 38%) were formed.

Example 55

[0194] The reaction was effected in the same manner as Example 44 except for using acetylacetonatomanganese(III) $\text{Mn}(\text{AA})_3$ instead of $\text{Co}(\text{AA})_2$. The conversion of adamantane was 66%, and 1-carboxyadamantane (yield 62%) was formed.

Example 56

[0195] The reaction was effected in the same manner as Example 44 except for using molybdic acid H_2MoO_4 instead of $\text{Co}(\text{AA})_2$. The conversion of adamantane was 58%, and 1-carboxyadamantane (yield 52%) was formed.

Example 57

[0196] The reaction was effected in the same manner as Example 44 except for using acetylacetonatoiron(III) $\text{Fe}(\text{AA})_3$ instead of $\text{Co}(\text{AA})_2$. The conversion of adamantane was 52%, and 1-carboxyadamantane (yield 50%) was formed.

Example 58

[0197] The reaction was effected in the same manner as Example 44 except for using manganese acetate $\text{Mn}(\text{OAc})_2$ instead of $\text{Co}(\text{AA})_2$. The conversion of adamantane was 71%, and 1-carboxyadamantane (yield 66%) was formed.

Example 59

[0198] The reaction was effected in the same manner as Example 44 except for using 0.005 mmole of acetylacetonatomanganese(II) $\text{Mn}(\text{AA})_2$ and 0.001 mmole of $\text{Co}(\text{AA})_2$ instead of $\text{Co}(\text{AA})_2$. The conversion of adamantane was 74%, and 1-carboxyadamantane (yield 71%) was formed.

Example 60

[0199] The reaction was effected in the same manner as Example 44 except for using acetylacetonatonickel(III) $\text{Ni}(\text{AA})_2$ instead of $\text{Co}(\text{AA})_2$. The conversion of adamantane was 51%, and 1-carboxyadamantane (yield 47%) was formed.

Example 61

[0200] The reaction was effected in the same manner as Example 44 except for using acetylacetonatochromium(III) $\text{Cr}(\text{AA})_3$ instead of $\text{Co}(\text{AA})_2$. The conversion of adamantane was 62%, and 1-carboxyadamantane (yield 60%) was formed.

Example 62

[0201] The reaction was effected in the same manner as Example 44 except for using acetylacetonatocopper(II) $\text{Cu}(\text{AA})_2$ instead of $\text{Co}(\text{AA})_2$. The conversion of adamantane was 47%, and 1-carboxyadamantane (yield 41%) was formed.

Example 63

[0202] The reaction was effected in the same manner as Example 44 except for using acetylacetonatocopper(III) $\text{Cu}(\text{AA})_3$ instead of $\text{Co}(\text{AA})_2$. The conversion of adamantane was 48%, and 1-carboxyadamantane (yield 43%) was

formed.

Example 64

- 5 **[0203]** The reaction was effected in the same manner as Example 44 except for using 1-carboxyadamantane instead of adamantane. The conversion of 1-carboxyadamantane was 80%, and 1,3-dicarboxyadamantane (yield 70%) was formed.

10 White solid
Mass spectral data $[M]^+$: 224
IR(cm^{-1}) : 3010, 1630, 1140

Comparative example 1

- 15 **[0204]** The stirring was carried out in the same manner as Example 44 without use of NHPI. No carboxyadamantane was detected.

Comparative example 2

- 20 **[0205]** The stirring was carried out in the same manner as Example 44 without use of oxygen. No carboxyadamantane was detected.

Example 65

- 25 **[0206]** To an autoclave, 10 mmole of 1,3-dinitroadamantane obtained by the method of Example 16, 5% Pd-C (10 mole% of Pd relative to a substrate), 1ml of dilute hydrochloric acid and 10ml of methanol were charged. The mixture was stirred for 2 hours at 80°C in an atmosphere of hydrogen at 30 atm. As a result, the conversion of 1,3-dinitroadamantane was 99%, and 1,3-diaminoadamantane (yield 95%) was formed.

30 Pale yellow solid
Mass spectral data $[M]^+$: 166
IR(cm^{-1}) : 3310, 1520, 870

Example 66

- 35 **[0207]** The reaction was effected in the same manner as Example 65 except for using Raney nickel (5 mole% of Ni relative to a substrate) instead of 5% Pd-C and that reacting for 4 hours. The conversion of 1,3-dinitroadamantane was 99%, and 1-amino-3-nitroadamantane (yield 80%) was formed.

40 Pale yellow solid
Mass spectral data $[M]^+$: 166
IR(cm^{-1}) : 3310, 1520, 870

Example 67

- 45 **[0208]** In an atmosphere of nitrogen, 11 mmole of acetyl chloride and 12 mmole of triethylamine were dissolved in 2 ml of tetrahydrofuran (THF). To the resultant solution, 10 mmole of 1-amino-3-nitroadamantane obtained by the method of Example 66 and 10 ml of N,N-dimethylformamide (DMF) were added. The mixture was stirred for 3 hours at 40°C. As a result, the conversion of 1-amino-3-nitroadamantane was 99%, and 1-acetylamino-3-nitroadamantane
50 (yield 95%) was formed.

Pale yellow liquid
Mass spectral data $[M]^+$: 238
IR(cm^{-1}) : 1680, 1550, 680
55

Example 68

- [0209]** In an atmosphere of nitrogen, 10 mmole of 1-carboxy-3-nitroadamantane obtained by the method of Example

42 was dissolved in 10ml of DMF. To the mixture, 15 mmole of acetyl chloride was added dropwise over 30 minutes. The mixture was heated to begin to reflux around the conclusion of the addition. After refluxing for 2 hours, the mixture was cooled, 20 mmole of triethylamine was added, and then 11 mmole of methanol was added dropwise over 30 minutes while retaining the temperature of the mixture at 10°C or less followed by stirring for more 2 hours. As a result, the conversion of 1-carboxy-3-nitroadamantane was 99%, and 1-methoxycarbonyl-3-nitroadamantane (yield 95%) was formed.

Pale yellow solid

Mass spectral data [M]⁺: 239

IR(cm⁻¹) : 1730, 1560, 1120

Example 69

[0210] In an atmosphere of nitrogen, 10 mmole of 1-carboxy-3-nitroadamantane obtained by the method of Example 43 was dissolved in 10ml of DMF. To the mixture, 15 mmole of acetyl chloride was added dropwise over 30 minutes. The mixture was heated to begin to reflux around the conclusion of the addition. After refluxing for 2 hours, the mixture was cooled, and 25 mmole of dimethylamine was added dropwise over 30 minutes while retaining the temperature of the mixture at 10°C or less followed by stirring for more 2 hours. As a result, the conversion of 1-carboxy-3-nitroadamantane was 99%, and 1-(N,N-dimethylcarbamoyl)-3-nitroadamantane (yield 95%) was formed.

Pale yellow solid

Mass spectral data [M]⁺: 252

IR(cm⁻¹) : 1660, 1560, 690

Example 70

[0211] The operation was effected in the same manner as Example 57 except for using 1-carboxy-3-nitroadamantane obtained by the method of Example 42 instead of 1,3-dinitroadmantane. The conversion of 1-carboxy-3-nitroadamantane was 80%, and 1-amino-3-carboxyadamantane (yield 70%) was formed.

Pale yellow solid

Mass spectral data [M]⁺: 195

IR(cm⁻¹) : 3370, 3000, 1670, 1620

Example 71

[0212] The operation was effected in the same manner as Example 67 except for using 1-amino-3-carboxyadamantane obtained by the method of Example 70 instead of 1-amino-3-nitroadmantane. The conversion of 1-amino-3-carboxyadamantane was 99%, and 1-acetylamino-3-carboxyadamantane (yield 95%) was formed.

Pale yellow liquid

Mass spectral data [M]⁺: 234

IR(cm⁻¹) : 3360, 1670, 1640

Example 72

[0213] The operation was effected in the same manner as Example 68 except for using 1,3-dicarboxyadamantane obtained by the method of Example 64 instead of 1-carboxy-3-nitroadmantane. The conversion of 1,3-dicarboxyadamantane was 90%, and 1-carboxy-3-methoxycarbonyladamantane (yield 80%) was formed.

White solid

Mass spectral data [M]⁺: 238

IR(cm⁻¹) : 3030, 1670, 1630

Example 73

[0214] In an atmosphere of nitrogen, 15 mmole of lithium aluminum hydride was suspended in 15 ml of THF. To the mixture, 10 mmole of 1,3-dicarboxyadamantane obtained by the method of example 64 was added slowly while retain-

ing the temperature of the mixture at 10 °C or less with use of an ice bath. After warming to the room temperature, the mixture was refluxed for 16 hours. As a result, The conversion of 1,3-dicarboxyadamantane was 90%, and 1-carboxy-3-hydroxymethyladamantane (yield 80%) was formed.

5 White solid
Mass spectral data $[M]^+$: 210
IR(cm^{-1}) : 3350, 3000, 1650

Example 74

10 [0215] The operation was effected in the same manner as Example 69 except for using 1,3-dicarboxyadamantane obtained by the method of Example 64 instead of 1-carboxy-3-nitroadmantane. The conversion of 1,3-dicarboxyadamantane was 90%, and 1-carboxy-3-(N,N-dimethylcarbamoyl)adamantane (yield 80%) was formed.

15 Pale yellow solid
Mass spectral data $[M]^+$: 251
IR(cm^{-1}) : 3010, 1670, 1630

Example 75

20 [0216] The operation was effected in the same manner as Example 67 except for using 1,3-diaminoadamantane obtained by the method of Example 65 instead of 1-amino-3-nitroadmantane. The conversion of 1,3-diaminoadamantane was 90%, and 1-acetylamino-3-aminoadamantane (yield 80%) was formed.

25 Pale yellow liquid
Mass spectral data $[M]^+$: 208
IR(cm^{-1}) : 3350, 1660, 760

Example 76

30 [0217] The operation was effected in the same manner as Example 68 except for using 1-amino-3-carboxyadamantane obtained by the method of Example 70 instead of 1-carboxy-3-nitroadmantane. The conversion of 1-amino-3-carboxyadamantane was 99%, and 1-amino-3-methoxycarbonyladamantane (yield 95%) was formed.

35 Pale yellow solid
Mass spectral data $[M]^+$: 209
IR(cm^{-1}) : 3330, 1630, 770

Example 77

40 [0218] The operation was effected in the same manner as Example 66 except for using 1-hydroxymethyl-3-nitroadmantane obtained by the method of Example 43 instead of 1,3-dinitroadmantane. The conversion of 1-hydroxymethyl-3-nitroadmantane was 99%, and 1-amino-3-hydroxymethyladamantane (yield 95%) was formed.

45 Pale yellow solid
Mass spectral data $[M]^+$: 181
IR(cm^{-1}) : 3300, 1160, 760

Example 78

50 [0219] The operation was effected in the same manner as Example 66 except for using 1-(N,N-dimethylcarbamoyl)-3-nitroadmantane obtained by the method of Example 69 instead of 1,3-dinitroadmantane. The conversion of 1-(N,N-dimethylcarbamoyl)-3-nitroadmantane was 90%, and 1-amino-3-(N,N-dimethylcarbamoyl) adamantane (yield 80%) was formed.

55 Pale yellow solid
Mass spectral data $[M]^+$: 222
IR(cm^{-1}) : 3310, 1670, 1140

Example 79

[0220] The operation was effected in the same manner as Example 68 except for using 1-acetylamino-3-carboxyadamantane obtained by the method of Example 71 instead of 1-carboxy-3-nitroadmantane. 1-acetylamino-3-methoxycarbonyladamantane (yield 80%) was formed. The conversion of 1-acetylamino-3-carboxyadamantane was 90%.

Pale yellow liquid

Mass spectral data $[M]^+$: 251

IR(cm^{-1}) : 3300, 1660, 1620

Example 80

[0221] The operation was effected in the same manner as Example 67 except for using 1-amino-3-hydroxymethyladamantane obtained by the method of Example 77 instead of 1-amino-3-nitroadmantane. The conversion of 1-amino-3-hydroxymethyladamantane was 90%, and 1-acetylamino-3-hydroxymethyladamantane (yield 80%) was formed.

Pale yellow liquid

Mass spectral data $[M]^+$: 223

IR(cm^{-1}) : 3310, 1650, 1160

Example 81

[0222] The operation was effected in the same manner as Example 67 except for using 1-amino-3-(N,N-dimethylcarbamoyl)adamantane obtained by the method of Example 78 instead of 1-amino-3-nitroadmantane. The conversion of 1-amino-3-(N,N-dimethylcarbamoyl)adamantane was 90%, and 1-acetylamino-3-(N,N-dimethylcarbamoyl)adamantane (yield 80%) was formed.

Pale yellow solid

Mass spectral data $[M]^+$: 264

IR(cm^{-1}) : 3300, 1670, 1650, 740

Example 82

[0223] The operation was effected in the same manner as Example 68 except for using 1-hydroxymethyl-3-carboxyadamantane obtained by the method of Example 73 instead of 1-carboxy-3-nitroadmantane. The conversion of 1-hydroxymethyl-3-carboxyadamantane was 90%, and 1-hydroxymethyl-3-methoxycarbonyladamantane (yield 80%) was formed.

White solid

Mass spectral data $[M]^+$: 224

IR(cm^{-1}) : 3310, 1620, 1430

Example 83

[0224] In an atmosphere of nitrogen, 22 mmole of acetyl chloride and 24 mmole of triethylamine were dissolved in 2 ml of tetrahydrofuran (THF). To the resultant solution, 10 ml of solution containing 10 mmole of 1,3-diaminoadamantane obtained by the method of Example 65 in N,N-dimethylformamide (DMF) was added and then stirred for 3 hours at 40°C. As a result, the conversion of 1,3-diaminoadamantane was 99%, and 1,3-bis(acetylamino)adamantane (yield 95%) was formed.

Pale yellow liquid

Mass spectral data $[M]^+$: 250

IR(cm^{-1}) : 3330, 1660, 1240

Example 84

[0225] In an atmosphere of nitrogen, 10 mmole of 1,3-dicarboxyadamantane obtained by the method of Example 64 was dissolved in 10 ml of DMF. To the mixture, 30 mmole of thionyl chloride was added dropwise over 30 minutes and

the mixture was heated to begin to reflux around the conclusion of addition. After refluxing for 2 hours, the mixture was cooled. To the mixture, 40 mmole of triethylamine was added followed by 22 mmole of methanol over 30 minutes while retaining the temperature of the mixture at 10°C or less, and then stirred for more 2 hours. As a result, the conversion of 1,3-dicarboxyadamantane was 99%, and 1,3-bis(methoxycarbonyl)adamantane (yield 95%) was formed.

5

White solid

Mass spectral data $[M]^+$: 252

IR(cm^{-1}) : 1620, 1240, 1030

10 Example 85

[0226] In an atmosphere of nitrogen, 30 mmole of lithium aluminum hydride was suspended in 15 ml of THF. To the mixture, 10 mmole of 1,3-dicarboxyadamantane obtained by the method of Example 64 was added slowly while retaining the temperature of the mixture at 10°C or less with use of a ice bath. After heating to the room temperature, the mixture was refluxed for 16 hours. As a result, the conversion of 1,3-dicarboxyadamantane was 99%, and 1,3-bis(hydroxymethyl)adamantane (yield 95%) was formed.

15

White solid

Mass spectral data $[M]^+$: 196

20 IR(cm^{-1}) : 3310, 1490, 720

Example 86

[0227] In an atmosphere of nitrogen, 10 mmole of 1,3-dicarboxyadamantane obtained by the method of Example 64 was dissolved in 10 ml of DMF. To the mixture, 30 mmole of thionyl chloride was added dropwise over 30 minutes and the mixture was heated to begin to reflux around the conclusion of addition. After refluxing for 2 hours, the mixture was cooled. To the mixture, 50 mmole of dimethylamine was added dropwise over 30 minutes while retaining the temperature of the mixture at 10°C or less, and then stirred for more 2 hours. As a result, the conversion of 1,3-dicarboxyadamantane was 99%, and 1,3-bis(N,N-dimethylcarbamoyl)adamantane (yield 95%) was formed.

30

Pale yellow solid

Mass spectral data $[M]^+$: 278

IR(cm^{-1}) : 1670, 1420, 1170

35 Example 87

[0228] 1 mmole of 1,3-bis(methoxycarbonyl)adamantane obtained by the method of Example 84 was dissolved in 30 ml of THF. To the mixture, 0.5mmole of dimethylamine and 0.1 mmole of aluminum chloride anhydride AlCl_3 was added and reacted for 6 hours at 80°C. As a result, The conversion of 1,3-bis(methoxycarbonyl)adamantane was 90%, and 1-methoxycarbonyl-3-(N,N-dimethylcarbamoyl)adamantane (yield 80%) was formed.

40

Pale yellow solid

Mass spectral data $[M]^+$: 265

IR(cm^{-1}) : 1670, 1630, 1170

45

Example 88

[0229] In an atmosphere of nitrogen, 10 mmole of 1-carboxy-3-hydroxymethyladamantane obtained by the method of Example 73 was dissolved in 10 ml of DMF. To the mixture, 15 mmole of N,N'-carbodiimidazol in the form of powder was added in one portion. After stirring for 1 hour at the room temperature, 15 mmole of dimethylamine and 15 mmole of diazabicycloundecene were added. The mixture was heated to 100°C and stirred for 8 hours. As a result, the conversion of 1-carboxy-3-hydroxymethyladamantane was 99%, and 1-hydroxymethyl-3-(N,N-dimethylcarbamoyl)adamantane (yield 95%) was formed.

50

55

Pale yellow liquid

Mass spectral data $[M]^+$: 237

IR(cm^{-1}) : 3310, 1660, 1220

Example 89

[0230] 10 mmole of 1-amino-3-nitroadamantane obtained by the method of Example 66 was dissolved in toluene (100ml). To the resultant solution, 12 mmole of phosgene was added at the room temperature and stirred for 6 hours. As a result, The conversion of 1-amino-3-nitroadamantane was 99%, and 1-isocyanato-3-nitroadamantane (yield 90%) was formed.

Pale yellow liquid

Mass spectral data $[M]^+$: 222

IR(cm^{-1}) : 2200, 1560, 1330, 750

Example 90

[0231] The operation was effected in the same manner as Example 89 except for using 1-aminoadamantane instead of 1-amino-3-nitroadamantane. The conversion of 1-aminoadamantane was 99%, and 1-isocyanatoadamantane (yield 90%) was formed.

Pale yellow liquid

Mass spectral data $[M]^+$: 177

IR(cm^{-1}) : 3300, 2180, 1270

Example 91

[0232] The operation was effected in the same manner as Example 80 except for using 1,3-diaminoadamantane obtained by the method of Example 65 instead of 1-amino-3-nitroadamantane. The conversion of 1,3-diaminoadamantane was 90%, and 1-isocyanatoadamantane (yield 80%) was formed.

Pale yellow liquid

Mass spectral data $[M]^+$: 192

IR(cm^{-1}) : 3310, 2270, 1520, 870.

Example 92

[0233] The operation was effected in the same manner as Example 89 except for using 1-amino-3-(N,N-dimethylcarbamoyl)adamantane obtained by the method of Example 78 instead of 1-amino-3-nitroadamantane. The conversion of 1-amino-3-(N,N-dimethylcarbamoyl)adamantane was 95%, and 1-isocyanato-3-(N,N-dimethylcarbamoyl)adamantane (yield 85%) was formed.

Pale yellow liquid

Mass spectral data $[M]^+$: 248

IR(cm^{-1}) : 2200, 1640, 1310, 750

Example 93

[0234] The operation was effected in the same manner as Example 89 except for using 1-amino-3-methoxycarbonyladamantane obtained by the method of Example 78 instead of 1-amino-3-nitroadamantane. The conversion of 1-amino-3-methoxycarbonyladamantane was 95%, and 1-isocyanato-3-methoxycarbonyladamantane (yield 85%) was formed.

Pale yellow liquid

Mass spectral data $[M]^+$: 235

IR(cm^{-1}) : 2220, 1640, 1330, 770

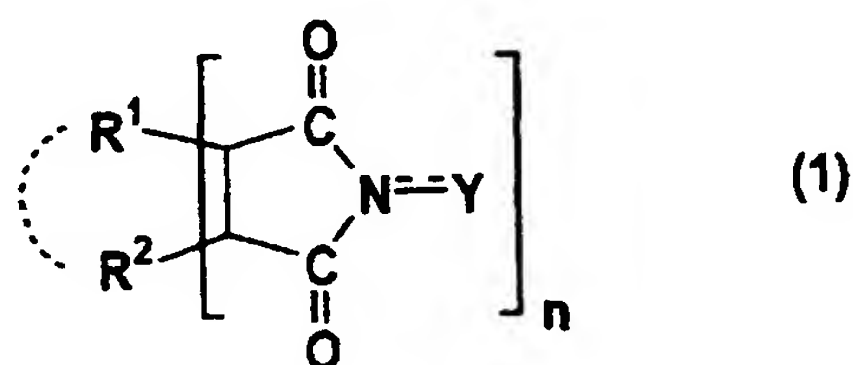
Example 94

[0235] To the mixture of 10 mmole of adamantane, 1 mmole of NHPI, 0.005 mmole of $\text{Co}(\text{AA})_2$ and 25 ml of acetic acid, nitrogen monoxide (NO), carbon monoxide (CO) and oxygen (O_2) were introduced in the ratio of NO:CO: O_2 (molar ratio)=10:15:1 at the pressure of 26kg/cm^2 and then stirred for 6 hours at 100°C . The reaction products were analyzed by gas chromatography and gas-mass spectrum apparatus, and as a result, 1,3,5-trinitroadamantane (yield 5%), 1-car-

boxy-3,5-dinitroadamantane (yield 5%), 1,3-dicarboxy-5-nitroadamantane (yield 1%) and 1,3,5-tricarboxyadamantane (yield 1%) were formed.

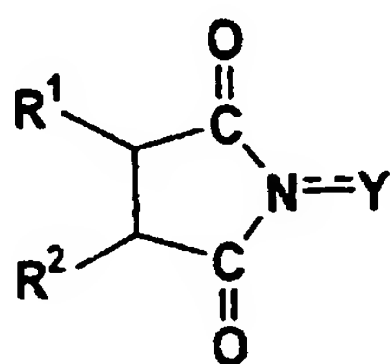
Claims

1. A catalyst for introducing at least one functional group selected from a nitro group and a carboxyl group to a substrate by contacting said substrate with at least one reactant selected from (i) a nitrogen oxide and (ii) a mixture of carbon monoxide and oxygen, which comprises an imide compound shown by the following formula (1):

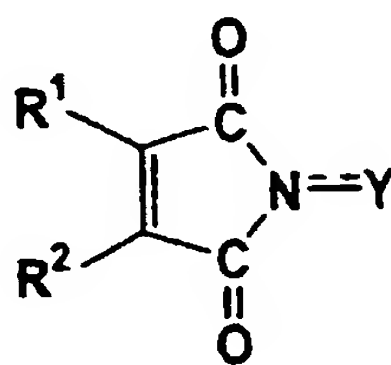


wherein R^1 and R^2 may be the same or different from each other, and represent a hydrogen atom, a halogen atom, an alkyl group, an aryl group, a cycloalkyl group, a hydroxyl group, an alkoxy group, a carboxyl group, an alkoxy carbonyl group, and an acyl group, and R^1 and R^2 may bond together to form a double bond, or an aromatic or non-aromatic ring; Y represents an oxygen atom or a hydroxyl group; and n denotes an integer of 1 to 3.

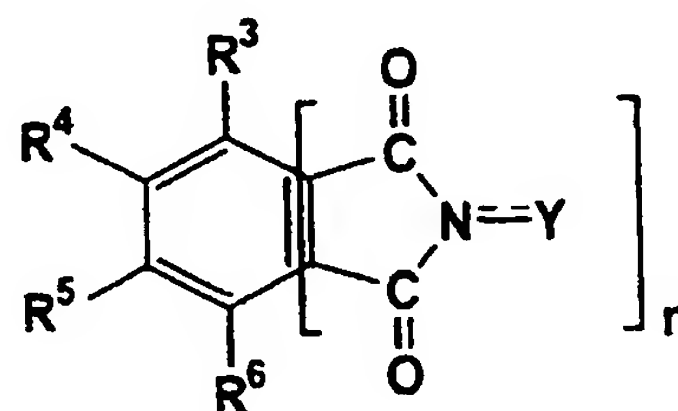
2. A catalyst according to claim 1, wherein R^1 and R^2 , in said imide compound shown by the formula (1), bond together to form an aromatic or non-aromatic 5 to 12 membered ring.
3. A catalyst according to claim 1, wherein R^1 and R^2 , in said imide compound shown by the formula (1), bond together to form a cycloalkane ring which may have a substituent, a cycloalkene ring which may have a substituent, a bridged hydrocarbon ring which may have a substituent or an aromatic ring which may have a substituent.
4. A catalyst according to claim 1, wherein said imide compound shown by the formula (1) is a compound shown by the following formulas (1a), (1b), (1c), (1d), (1e) and (1f):



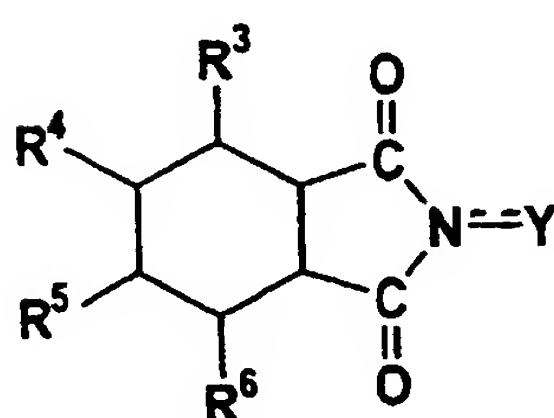
(1a)



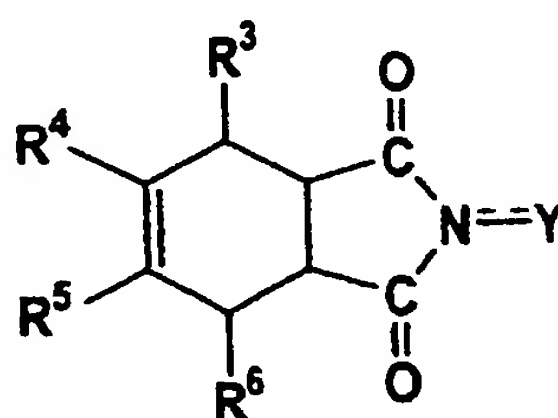
(1b)



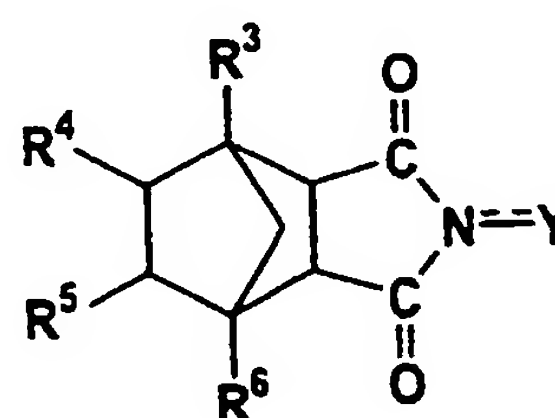
(1c)



(1d)



(1e)

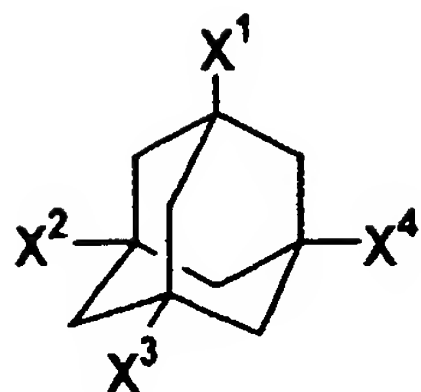


(1f)

wherein R^3 , R^4 , R^5 and R^6 are the same or different from each other, and represent a hydrogen atom, an alkyl group, a hydroxyl group, an alkoxy group, a carboxyl group, an alkoxy carbonyl group, an acyl group, a nitro

group, a cyano group, an amino group or a halogen atom; and R^1 , R^2 , Y and n have the same meanings as defined above.

5. A catalyst according to claim 1, wherein said imide compound shown by the formula (1) is at least one compound selected from the group consisting of N-hydroxysuccinimide, N-hydroxymaleimide, N-hydroxyhexahydrophthalimide, N,N'-dihydroxycyclohexanetetracarboximide, N-hydroxyphthalimide, N-hydroxytetrabromophthalimide, N-hydroxytetrachlorophthalimide, N-hydroxyhetimide, N-hydroxyhimimide, N-hydroxytrimellitide, N,N'-dihydroxypyromellitide and N,N'-dihydroxynaphthalenetetracarboximide.
6. A catalyst according to claim 1, which comprises said imide compound shown by the formula (1) and a co-catalyst.
7. A catalyst according to claim 6, wherein said co-catalyst is a compound containing at least one element selected from the group consisting of Group 2A elements of the Periodic Table of Elements, transition metal elements and Group 3B elements of the Periodic Table of Elements.
8. A catalyst according to claim 8, wherein said co-catalyst is a compound containing at least one element selected from the group consisting of Group 3A elements, Group 4A elements, Group 5A elements, Group 6A elements, Group 7A elements, Group 8 elements, Group 1B elements and Group 2B elements of the Periodic Table of Elements.
9. A catalyst according to claim 6, wherein the ratio of said co-catalyst to said imide compound shown by the formula (1) is 0.001 to 10 mole of the co-catalyst relative to 1 mole of the imide compound.
10. A process comprises contacting a substrate with at least one reactant selected from (i) a nitrogen oxide and (ii) a mixture of carbon monoxide and oxygen at least in the presence of the catalyst according to claim 1 to introduce at least one functional group selected from a nitro group and a carboxyl group to the substrate.
11. A process according to claim 10, said substrate is a member selected from (a) a compound having a methyl group or a methylene group at an adjacent site of an unsaturated bond, (b) a homo- or hetero cyclic compound having a methylene group, (c) a compound having a methine carbon atom, (d) a compound having a methyl group or a methylene group at an adjacent site of an aromatic ring and (e) a compound having a methylene group at an adjacent site of a carbonyl group.
12. A process according to claim 10, said substrate is a compound having a methine carbon atom or a compound having a methyl or methylene group at a benzyl site of the compound.
13. A process according to claim 10, wherein said nitrogen oxide is shown by the formula:
$$N_xO_y$$
wherein x denotes an integer of 1 or 2 and y denotes an integer of 1 to 6.
14. A process according to claim 10, wherein said nitrogen oxide comprises at least one nitrogen compound selected from N_2O_3 and NO_2 as a main component.
15. A process according to claim 10, wherein not less than 1 mole of carbon monoxide and not less than 0.5 mole of oxygen relative to 1 mole of said substrate are employed.
16. A process according to claim 10, a ratio of carbon monoxide to oxygen is carbon monoxide/oxygen = about 1/99 to 99.99/0.01 (mole ratio).
17. A process for producing a compound having at least one functional group selected from a nitro group and a carboxyl group, which comprises, at least in the presence of the catalyst according to claim 1, contacting a substrate with at least one reactant selected from (i) a nitrogen oxide and (ii) a mixture of carbon monoxide and oxygen.
18. An adamantane derivative shown by the following formula (2):



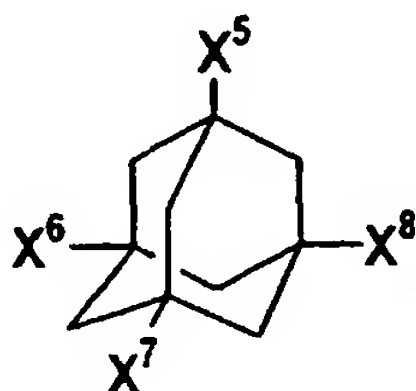
(2)

wherein X¹ represents a nitro group, an amino group or N-substituted amino group which may be protected by a protective group, a carboxyl group which may be protected by a protective group, or a hydroxymethyl group which may be protected by a protective group; and X³ and X⁴ may be the same or different from each other, and represents a hydrogen atom, an alkyl group, a nitro group, an amino group or N-substituted amino group which may be protected by a protective group, a carboxyl group which may be protected by a protective group, a hydroxymethyl group which may be protected by a protective group or an isocyanato group;

- (i) when X¹ is a nitro group, X² represents an amino group or N-amino group which may be protected by a protective group, a hydroxymethyl group which may be protected by a protective group, or an isocyanato group;
- (ii) when X¹ is an amino group or N-substituted amino group which may be protected by a protective group, X² represents an isocyanato group;
- (iii) when X¹ is a carboxyl group which may be protected by a protective group, X² represents a hydroxymethyl group which may be protected by a protective group, or an isocyanato group; and
- (iv) when X¹ is a hydroxymethyl group which may be protected by a protective group, X² represents an isocyanato group;

or a salt thereof.

19. An adamantane derivative shown by the following formula (3):



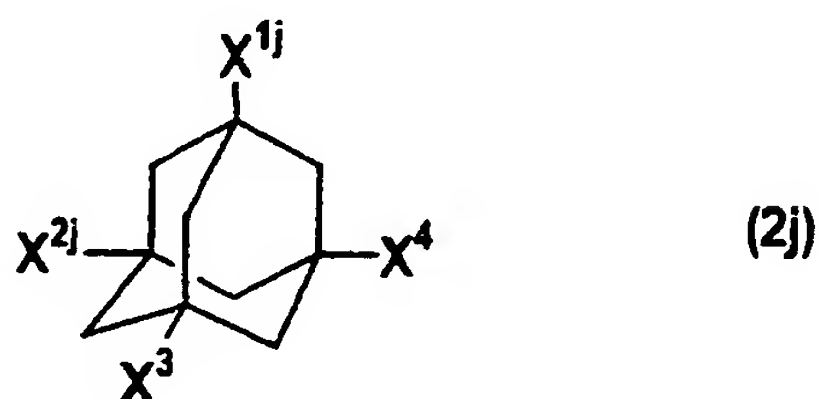
(3)

wherein X⁵ represents a carbamoyl group which may have a substituent, a nitro group, a substituted hydroxycarbonylamino group, or a saturated aliphatic acylamino group or aromatic acylamino group; X⁷ and X⁸ are the same or different from each other, and represent a hydrogen atom, an alkyl group, a nitro group, an amino or N-substituted amino group which may be protected by a protective group, a carboxyl group which may be protected by a protective group, a hydroxymethyl group which may be protected by a protective group, or an isocyanato group;

- (i) when X⁵ is a carbamoyl group which may have a substituent, X⁶ represents a carboxyl group, a substituted hydroxycarbonyl group, an amino group or N-substituted amino group which may be protected by a protective group, or a nitro group;
- (ii) when X⁵ is a nitro group, X⁶ represents a substituted hydroxycarbonyl group;
- (iii) when X⁵ is a substituted hydroxycarbonylamino group, X⁶ represents a substituted hydroxycarbonyl group, a hydroxymethyl group which may be protected by a protective group, or an amino group which may be protected by a protective group; and
- (iv) X⁵ is a saturated aliphatic acylamino group or aromatic acylamino group, X⁶ represents a carboxyl group, a hydroxymethyl group which may be protected by a protective group, or an amino group which may be substituted by an alkyl group;

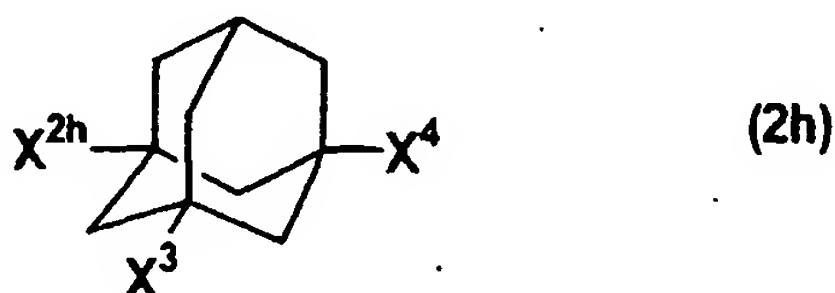
or a salt thereof.

20. A process for producing a diaminoadamantane derivative shown by the following formula (2j):

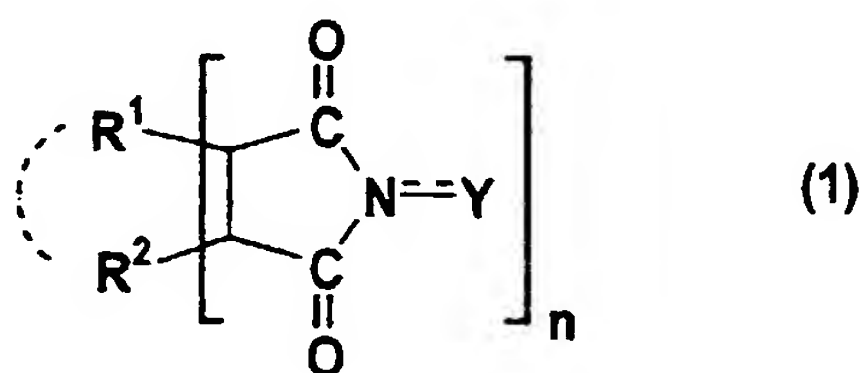


15 wherein X^{1j} and X^{2j} represent an amino group or N-substituted amino group which may be protected by a protective group; and X^3 and X^4 are the same or different from each other, and represent a hydrogen atom, an alkyl group, a nitro group, an amino group or N-substituted amino group which may be protected by a protective group, a carboxyl group which may be protected by a protective group, a hydroxymethyl group which may be protected by a protective group, or an isocyanato group; or a salt thereof, which comprises the steps of

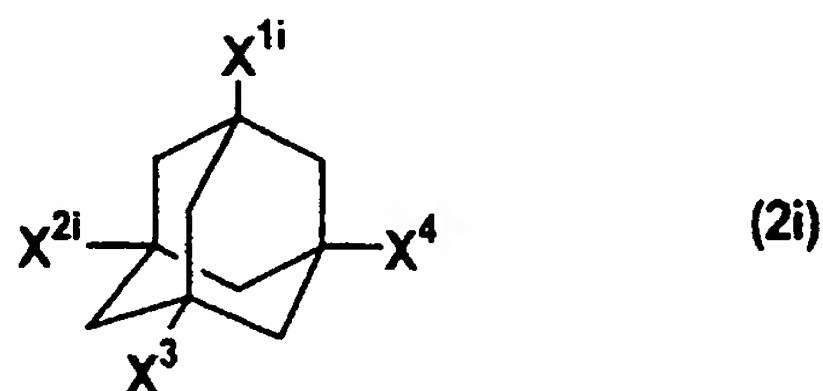
20 contacting a compound shown by the following formula (2h):



30 wherein X^{2h} represents a hydrogen atom or a nitro group; X^3 and X^4 have the same meanings as defined above; with a nitrogen oxide, in the presence of an imide compound shown by the following formula (1):



45 wherein R^1 and R^2 are the same or different from each other, and represents a hydrogen atom, a halogen atom, an alkyl group, an aryl group, a cycloalkyl group, a hydroxyl group, an alkoxy group, a carboxyl group, an alkoxycarbonyl group, and an acyl group; R^1 and R^2 may bond together to form a double bond, or an aromatic or non-aromatic ring; Y represents an oxygen atom or a hydroxyl group; and n denotes an integer of 1 to 3, to produce a dinitroadamantane derivative shown by the following formula (2i):



wherein X^{1i} and X^{2i} each represents a nitro group; and X^3 and X^4 have the same meanings as defined above; and

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reducing said dinitroadamantane derivative shown by the formula (2i) to produce a corresponding diamino compound.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP98/00079

A. CLASSIFICATION OF SUBJECT MATTER

Int.Cl⁶ B01J31/02, B01J31/26, C07C201/08, C07C51/10, C07C61/28,
C07C211/35, C07C265/10, C07C205/55, C07C62/06, C07C271/24,

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Int.Cl⁶ B01J31/02, B01J31/26, C07C201/08, C07C51/10, C07C61/28,
C07C211/35, C07C265/10, C07C205/55, C07C62/06, C07C271/24,

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Jitsuyo Shinan Koho 1926-1996 Toroku Jitsuyo Shinan Koho 1994-1997
Kokai Jitsuyo Shinan Koho 1971-1997 Jitsuyo Shinan Keisai Koho 1996-1997

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAPLUS (STN), REGISTRY (STN)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JP, 7-074168, B (F. Hoffmann-La Roche AG.), August 9, 1995 (09. 08. 95), Page 2, column 3, line 41 to column 4, line 3 ; page 2, column 4, line 40 to page 3, column 5, line 1 & EP, 198351, A & DE, 3666417, G & DK, 8601451, A & US, 5030739, A	1-5
X	Gilardi, Richard et al., "Structure of 1-amino- 3,5,7-trinitroadamantane", Acta Crystallogr., Sect. C: Cryst. Struct. Commun. (1991), C47(9), pp.1914-1916	18
X	Zajac, Walter W. et al., "1-Amino-3,5,7- trinitroadamantane: an unexpected oxidation product of 1,3,5,7-tetraaminoadamantane. An improved synthesis of 1,3,5,7-tetranitroadamantane.", J. Org. Chem. (1989), 54(10), pp.2468-2471	18

☒ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document but published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search
April 28, 1998 (28. 04. 98)

Date of mailing of the international search report
May 19, 1998 (19. 05. 98)

Name and mailing address of the ISA/
Japanese Patent Office

Authorized officer

Facsimile No.

Telephone No.

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP98/00079

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Khil'chevskii, A. N. et al., "Reaction of adamantane and adamantane- and bicyclo[3.3.1]nonane-type carboxylic acids with acetonitrile in liquid bromine", Zh. Org. Khim. (1996), 32(7), pp.1022-1024	19
X	Mella, M. et al., "Oxidative Functionalization of Adamantane and Some of Its Derivatives in Solution", J. Org. Chem. (1996), 61(4), pp.1413-1422	19
X	JP, 56-092847, A (G.D. Searle & Co.), July 27, 1981 (27. 07. 81), Claims ; Examples & DE, 3044793, A & US, 4273704, A & NL, 8006586, A & NO, 8003640, A & SE, 8008428, A & FR, 2476073, A & DK, 8005134, A & IT, 1127930, A & GB, 2066262, B	19
X	Stepanov, F. N. et al., "Adamantane and its derivatives. VIII. Synthesis and acid hydrolysis of tri- and tetra-substituted acylamino derivatives of adamantane.", Zh. Org. Khim. (1966), 2(9), pp.1612-1615	19
X	Vishnevskii, E. N. et al., "Nitration of adamantane by nitrogen dioxide", Zh. Org. Khim. (1996), 32(7), pp.1030-1035	19
X	JP, 56-071075, A (Sumitomo Chemical Co., Ltd.), June 13, 1981 (13. 06. 81) & DK, 8004801, A & US, 4332806, A & EP, 28936, A	19
PX	JP, 9-143109, A (Ube Industries, Ltd.), June 3, 1997 (03. 06. 97), Page 2, column 1, line 47 to column 2, line 38 (Family: none)	1-9
PX	JP, 9-278675, A (Daicel Chemical Industries, Ltd.), October 28, 1997 (28. 10. 97), Page 4, column 5, line 25 to column 6, line 11 ; page 5, column 7, line 8 to page 8, column 14, line 31 & WO, 9728897, A & EP, 924962, A	1-9

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP98/00079

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

The compounds represented by the general formula described in claim 18 or 19 exhibit neither the properties nor the activities in common to each other as a raw material, intermediate or final product, and therefore claim 18 or 19 which describes compounds having no properties in common to each other in the form of one claim lacks in unity.

Claim 20 is not a process comprising the step of isocyanation, hydroxymethylation or carbamoylation, and therefore does not relate to a process for the preparation of the compounds represented by the formula described in claim 18 or 19, though it relates to a process for the preparation of part of such compounds.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP98/00079

A. (Continuation) CLASSIFICATION OF SUBJECT MATTER

C07B43/02, C07B41/08

B. (Continuation) FIELDS SEARCHED

C07B43/02, C07B41/08